Clinical trial results:
A double-blind, randomised, placebo-controlled study on the Efficacy of Iberogast® (STW 5) in patients with functional dyspepsia and concomitant reflux symptoms measured with impedance and wireless pH monitoring

Summary

EudraCT number	2008-002305-40
Trial protocol	DE
Global end of trial date	03 May 2013

Results information

Result version number	v1 (current)
This version publication date	31 August 2019
First version publication date	31 August 2019

Trial information

Trial identification

Sponsor protocol code	BAY98-7411/20985

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.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	03 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 May 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To show the superiority of STW 5 compared to placebo for the treatment of patients with functional dyspepsia with concomitant reflux symptoms

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 June 2009
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	Germany: 63
Worldwide total number of subjects	63
EEA total number of subjects	63

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)	43
From 65 to 84 years	20

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In eight active centres in Germany, a total of 67 patients were screened for the study. Overall, 64 from the screened population were randomized, and 63 patients received treatment.

Pre-assignment

Screening details:

67 subjects were screened for the study. Overall, three patients from the screened population were not randomized, two of these did not meet the inclusion criteria, one patient discontinued prematurely due to 'other reason' (no pain).

Period 1

Period 1 title	Overall study (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	STW5

Arm description:

Subjects will take STW5 orally from day 0 to day 28. The dosage was 20 drops three times daily before the meals.

Arm type	Experimental
Investigational medicinal product name	STW-5
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops, solution
Routes of administration	Oral use

Dosage and administration details:

The medication was applied daily per os (orally, p.o.) from day 0 to day 28. The dosage was 20 drops three times daily before the meals.

Arm title	Placebo

Arm description:

Subjects will take Placebo orally from day 0 to day 28. The dosage was 20 drops three times daily before the meals.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral drops, solution
Routes of administration	Oral use

Dosage and administration details:

The medication was applied daily per os (orally, p.o.) from day 0 to day 28. The dosage was 20 drops three times daily before the meals.

Number of subjects in period 1	STW5	Placebo
Started	33	30
Completed	33	29
Not completed	0	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	STW5
Reporting group description:	
Subjects will take STW5 orally from day 0 to day 28. The dosage was 20 drops three times daily before the meals.	
Reporting group title	Placebo
Reporting group description:	
Subjects will take Placebo orally from day 0 to day 28. The dosage was 20 drops three times daily before the meals.	

Reporting group values	STW5	Placebo	Total
Number of subjects	33	30	63
Age categorical Units: Subjects			
Age continuous Units: years geometric mean standard deviation	 57.55 ± 16.266	 51.83 ± 13.414	 -
Gender categorical Units: Subjects			
Female	28	23	51
Male	5	7	12

End points

End points reporting groups

Reporting group title	STW5
Reporting group description:	
Subjects will take STW5 orally from day 0 to day 28. The dosage was 20 drops three times daily before the meals.	
Reporting group title	Placebo
Reporting group description:	
Subjects will take Placebo orally from day 0 to day 28. The dosage was 20 drops three times daily before the meals.	
Subject analysis set title	Safety set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All randomised patients who received at least one dose of study medication. The set included all patients exposed to study treatment.	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All randomised patients who received at least one dose of study medication and for whom post-randomisation data of efficacy is available. This set included patients with treatment effects measured, according to the intention-to-treat principle.	
Subject analysis set title	Per-protocol set
Subject analysis set type	Per protocol
Subject analysis set description:	
The per-protocol set included all patients from the full analysis set who essentially completed the study in compliance with the protocol and who reported no major violation of the study protocol. This might include but is not limited to meeting all inclusion criteria and not meeting any exclusion criteria, compliance with study treatment, and presenting with the required assessments of the primary target variable. The per-protocol set was the set of patients that participated in the trial as intended, according to the per-protocol principle.	

Primary: AUC of patients assessment of gastrointestinal symptoms

End point title	AUC of patients assessment of gastrointestinal symptoms
End point description:	
Area under the curve (AUC) of patients` assessment of gastrointestinal symptoms evaluated by daily visual analogue scale (VAS)	
End point type	Primary
End point timeframe:	
Up to 28 days	

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31[1]	27[2]		
Units: mm*days				
arithmetic mean (standard deviation)	88.3 (± 8.75)	85.9 (± 9.29)		

Notes:

[1] - 2 patients did not have post-treatment efficacy variable

[2] - 3 patients did not have post-treatment efficacy variable

Statistical analyses

Statistical analysis title	Superiority of STW 5 against placebo
Comparison groups	STW5 v Placebo
Number of subjects included in analysis	58
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8408
Method	ANCOVA

Secondary: Global Improvement Scale

End point title	Global Improvement Scale

End point description:

Assessed by Global Improvement Scale (substantially worsened/moderately worsened/ marginally worsened/not changed/ marginally improved/ moderately improved/ substantially improved).

End point type	Secondary

End point timeframe:

At day 28

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: Subjects				
number (not applicable)				
My complaints have substantially improved	8	9		
My complaints have moderately improved	7	5		
My complaints have marginally improved	3	3		
My complaints have not changed	8	4		
My complaints have marginally worsened	0	0		
My complaints have moderately worsened	1	2		
My complaints have substantially worsened	1	1		
Not available	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of the Gastrointestinal Symptoms Profile (GIS) from baseline (visit 3) at the day 28 (visit 5)

End point title	Change of the Gastrointestinal Symptoms Profile (GIS) from

	baseline (visit 3) at the day 28 (visit 5)

End point description:

The GIS is a symptom related score, validated in German language, which allows the investigator to assess the dyspeptic symptoms by asking the patient for the following 10 items (GIS): epigastric pain / upper abdominal pain, abdominal cramps, fullness, early satiety, loss of appetite, sickness, nausea, vomiting, retrosternal discomfort and acid eructation/heartburn. The total GIS score is 40 points and an increasing summary score therefore represents a higher intensity of dyspeptic symptoms

End point type	Secondary

End point timeframe:

At day 0 and day 28

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: Score				
arithmetic mean (standard deviation)				
Visit 3 (baseline)	12.9 (± 4.41)	12.4 (± 3.69)		
Visit 5	7.7 (± 5.00)	6.4 (± 5.63)		
Change from visit 5 to visit 3	-5.1 (± 3.75)	-6.0 (± 4.81)		

Statistical analyses

No statistical analyses for this end point

Secondary: AUC of reflux symptoms assessment measured by daily VAS scale

End point title	AUC of reflux symptoms assessment measured by daily VAS scale

End point description:

Area under the curve (AUC) of assessment of reflux symptoms evaluated by daily visual analogue scale (VAS). VAS is an s an unmarked scale on a line 100 mm in length, indicating from 0 mm (no symptoms) to 100 mm (severe symptoms)

End point type	Secondary

End point timeframe:

Up to 28 days

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: mm*days				
arithmetic mean (standard deviation)				
AUC of heartburn	51.40 (± 47.151)	49.63 (± 42.813)		
AUC of acid eructation	46.53 (± 47.905)	42.27 (± 36.350)		

Statistical analyses

No statistical analyses for this end point

Secondary: FDDQL total score and change from baseline at visit 5

End point title	FDDQL total score and change from baseline at visit 5

End point description:

The Functional Dyspepsia Quality of Life (FDDQL) provided a profile with eight subscores (daily activities, anxiety, diet, sleep, discomfort, health perceptions, coping with disease and impact of stress) as well as a global score. Sub-scale scores and the global score were transformed to a range from "0 = Poor QoL" to "100= Good QoL".

End point type	Secondary

End point timeframe:

At baseline and day 28 (visit 5)

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: Score				
arithmetic mean (standard deviation)				
Visit 3 (baseline)	42.5 (± 15.05)	45.3 (± 13.22)		
Visit 5	34.9 (± 15.97)	34.1 (± 14.21)		
Change from visit 5 to baseline	-7.5 (± 10.67)	-11.2 (± 15.58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Esophageal ph measurement using the BravoTM pH system and intraluminal impedance

End point title	Esophageal ph measurement using the BravoTM pH system and intraluminal impedance

End point description:

End point type	Secondary

End point timeframe:

BravoTM pH system: at day -7/ -5 (screening phase) and day 29/30 if applicable
Intraluminal impedance: at day -1 (screening phase) and day 29/30 if applicable

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: ph				
number (not applicable)				

Notes:

[3] - Due to few data available, no summary statistics or results of an ANCOVA can be presented

[4] - Due to few data available, no summary statistics or results of an ANCOVA can be presented.

Statistical analyses

No statistical analyses for this end point

Secondary: Global assessment of efficacy judged by patient using a five point Likert scale

End point title	Global assessment of efficacy judged by patient using a five point Likert scale

End point description:

1 = very good, 2 = good, 3 = moderate, 4 = poor, 5 = very poor

End point type	Secondary

End point timeframe:

At day 28

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: Subjects				
Very good	7	9		
Good	9	6		
Moderate	6	3		
Poor	6	7		
Very poor	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Global assessment of efficacy judged by physician using a five point Likert scale

End point title	Global assessment of efficacy judged by physician using a five point Likert scale

End point description:

1 = very good, 2 = good, 3 = moderate, 4 = poor, 5 = very poor

End point type	Secondary

End point timeframe:

At day 28

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: Subjects				
Very good	7	8		
Good	12	6		
Moderate	4	3		
Poor	6	9		
Very poor	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Change of Individual symptom score from baseline (visit 3) at day 28 (visit 5)

End point title	Change of Individual symptom score from baseline (visit 3) at day 28 (visit 5)

End point description:

The GIS sub-scores for epigastric pain (item 1) and reflux symptoms (item 10). The sub-scores were assessed and analysed using the following scores: 0 = No problem, 1 = Mild problem, 2 = Moderate problem, 3 = Severe problem, 4 = Very severe

End point type	Secondary

End point timeframe:

At baseline and day 28

End point values	STW5	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	27		
Units: Score				
arithmetic mean (standard deviation)				
Epigatric pain: visit 3 (baseline)	2.2 (± 0.72)	2.2 (± 0.75)		
Epigatric pain: visit 5	1.4 (± 0.88)	1.0 (± 0.98)		
Epigatric pain: change from visit 5 to visit 3	-0.9 (± 0.85)	-1.2 (± 0.92)		
Reflux system: visit 3 (baseline)	1.7 (± 0.74)	2.0 (± 0.78)		
Reflux system: visit 5	1.1 (± 0.68)	0.9 (± 0.89)		

Reflux system: change from visit 5 to visit 3	-0.6 (± 0.66)	-1.1 (± 1.25)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From day 0 to day 28 (end of study)	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0
Reporting groups	
Reporting group title	STW5
Reporting group description:	
Subjects will take STW5 orally from day 0 to day 28. The dosage was 20 drops three times daily before the meals.	
Reporting group title	Placebo
Reporting group description:	
Subjects will take Placebo orally from day 0 to day 28. The dosage was 20 drops three times daily before the meals.	

Serious adverse events	STW5	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	STW5	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 33 (15.15%)	7 / 30 (23.33%)	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Intercostal neuralgia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Nerve compression			

subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Dyspepsia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 33 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
Vomiting			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 January 2009	The address of principle investigator changed
22 January 2010	The BRAVO procedure was changed to voluntarily

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported