



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 | Investigator, Subject |

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 |
|-----------------|--|

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 (\pm 4.41) | 12.4 (\pm 3.69) | | |
| Visit 5 | 7.7 (\pm 5.00) | 6.4 (\pm 5.63) | | |
| Change from visit 5 to visit 3 | -5.1 (\pm 3.75) | -6.0 (\pm 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 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 (\pm 47.151) | 49.63 (\pm 42.813) | | |
| AUC of acid eructation | 46.53 (\pm 47.905) | 42.27 (\pm 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 Bravo™ pH system and intraluminal impedance

| | |
|-----------------|---|
| End point title | Esophageal pH measurement using the Bravo™ pH system and intraluminal impedance |
|-----------------|---|

End point description:

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

End point timeframe:

Bravo™ 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) | | | | |
| Epigastric pain: visit 3 (baseline) | 2.2 (± 0.72) | 2.2 (± 0.75) | | |
| Epigastric pain: visit 5 | 1.4 (± 0.88) | 1.0 (± 0.98) | | |
| Epigastric 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 (\pm 0.66) | -1.1 (\pm 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 occurrences (all) | 0 / 33 (0.00%) 0 | 1 / 30 (3.33%) 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