ISRCTN31630783 https://doi.org/10.1186/ISRCTN31630783

A clinical trial to investigate efficacy and safety of Menthacarin® in patients (at least 18 years old) suffering from symptoms of Irritable Bowel Syndrome (IBS)

Submission date
09/05/2016

Recruitment status
No longer recruiting

Registration date
17/05/2016

Overall study status
Completed

Last Edited
23/06/2020

Condition category
Digestive System

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Irritable bowel syndrome (IBS) is a common, long-term disorder of the digestive system. It is part of a group of disorders called functional bowel disorders, as it affects the way the bowel (intestines) functions. IBS is associated with a number of digestive symptoms such as abdominal pain, diarrhoea, constipation and flatulence, which can affect quality of life and social functioning. Studies have shown that Menthacarin®, a combination of peppermint oil and caraway oil, is effective in another common digestive system disorder called functional dyspepsia (which causes discomfort in the upper belly, near the ribs). These two syndromes, IBS and FD, have many overlapping symptoms (such as abdominal pain, bloating) and so Menthacarin® could also be effective for the treatment of IBS. The aim of this study is to investigate the efficacy of Menthacarin® in patients suffering from IBS.

Who can participate?
Adults with IBS.

What does the trial involve?
Participants are randomly allocated to one of four groups (A1, A2, B1, and B2). After a screening period (maximum of 10 consecutive days) participants are given capsules containing either Menthacarin® or placebo (dummy medication) to take everyday for the next eight weeks. After this, for four weeks, all participants receive capsules containing Menthacarin®. Each participant receives a follow-up phone call seven days after they take their last dose of medication.

What are the possible benefits and risks of participating?
Participants may benefit from a reduction in their IBS symptoms (such as abdominal pain and bloating) and an improvement in their quality of life. They may also benefit from the diagnostic measures (e.g. general physical examination, laboratory test, etc.) applied at their first, fourth, fifth and sixth scheduled visits. During blood sampling, a small risk of infection may occur, but this can be reduced by the use of adequate techniques. It is expected that the participants will

benefit from the treatment with Menthacarin® when they suffer from symptoms of IBS during the study. As Menthacarin® is well tolerated according to the data gathered so far, there is no major risk to taking Menthacarin®. Gastric complaints (mainly eructation) may occur during treatment with Menthacarin® in sensitive patients. In very rare cases, allergic reactions may also occur.

Where is the trial run from?
KRH Klinikum Siloah-Oststadt-Heidehaus and 19 other health centres (Germany)

When is the study starting and how long is it expected to run for?
February 2014 to March 2019

Who is funding the trial?
Dr. Willmar Schwabe GmbH & Co. KG (Germany)

Who is the main contact?
Professor Ahmed Madisch

Contact information

Type(s)
Scientific

Contact name
Prof Ahmed Madisch

Contact details
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Additional identifiers

Clinical Trials Information System (CTIS)
2014-004702-14

Protocol serial number
530079.01.302

Study information

Scientific Title
Efficacy and tolerability of Menthacarin® in patients (≥ 18 years old) suffering from symptoms of irritable bowel syndrome (IBS)

Study objectives
The aim of this study is to investigate if Menthacarin® is superior to placebo with respect to change in abdominal pain.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics Committee Niedersachsen, Hannover, 12/03/2015, ref: Bo 37/2014

Study design
Prospective multi-centre randomized, double-blind placebo-controlled phase III clinical trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Irritable bowel syndrome (IBS)

Interventions
All participants undergo following scheduled visits:

Visit 1: Day -10 (Screening)
Visit 2: Day 0 (Baseline)
Visit 3: 14 days ± 4 days after randomization
Visit 4: 28 days ± 4 days after randomization (End of double-blind treatment period)
Visit 5: 56 days ± 4 days after randomization (End of follow-up double-blind treatment period)
Visit 6: 84 days ± 4 days after randomization (End of follow-up treatment period)
Visit 7: 91 – 95 days after randomization (End of Post-treatment observation period)

The participants are randomly divided into four treatment groups (group A1, A2, B1, B2):

Double-blind treatment phase (for 28 consecutive days):
Groups A1 and A2: Active Medication (Menthacarin®) in the form of one soft capsule two times daily (Gastro-resistant soft capsules containing Menthacarin - proprietary combination of essential oils of a specified quality from Mentha x piperita L. (90 mg WS® 1340) and Carum carvi (50 mg WS® 1520)) as active ingredient)
Groups B1 and B2: Placebo: One soft capsule two times daily

Follow-up double-blind treatment period (for 28 consecutive days):
Group A1: Active Medication (Menthacarin®): one soft capsule two times daily
Group A2: Placebo: one soft capsule two times daily
Group B1: Active Medication (Menthacarin®): one soft capsule two times daily
Group B2: Placebo: one soft capsule two times daily

Follow-up open treatment period (for 28 consecutive days):
All groups: Active Medication (Menthacarin®): one soft capsule two times daily

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Menthacarin

Primary outcome(s)
Abdominal pain is measured using an 11 point numeric rating scale (NRS) between day -10 and day 28 (daily), according to the assessment of the patient as a part of the patient's diary.
The primary outcome will be the change in abdominal pain at day 28 in comparison to day 0 (weekly average of the patient's diary data) between Menthacarin groups and placebo groups.

Key secondary outcome(s))
1. Abdominal pain and symptoms, i.e. abdominal discomfort, abdominal cramping, abdominal fullness, and abdominal bloating, is measured using an 11 point numeric rating scale (NRS) between day -10 and day 84 (daily), according to the assessment of the patient as a part of the patient's diary
2. Illness severity is measured using the questionnaire Clinical Global Impression (Severity) (CGI-S) at day 0, day 14, day 28, day 56, and day 84, according to the assessment of the investigator
3. The global improvement or change is measured using the questionnaire Clinical Global Impression (Change) (CGI-C) at day 14, day 28, day 56, and day 84, according to the assessment of the investigator as well as at day 13, day 27, day 55, day 83 (one day before scheduled visit), according to the assessment of the patient as a part of the patient's diary
4. The improvement of IBS symptoms is measured using the questionnaire IBS global assessment of improvement (IBS-GAI) at day 13, day 27, day 55, day 83 (one day before scheduled visit), according to the assessment of the patient as a part of the patient's diary
5. IBS-specific Quality of life is measured using the IBS Quality of Life Questionnaire (IBS-QOL) at day 0, day 28, day 56, and day 84, according to the assessment of the patient (filled out by patient during the scheduled visits)
6. The severity of IBS symptoms is measured using the Irritable Bowel Syndrome Severity Scoring System (IBS-SSS) questionnaire at day 0, day 14, day 28, day 56, and day 84, according to the assessment of the patient (filled out by patient during the scheduled visits)
7. The Frequency of Spontaneous Bowel Movements (SBMs) is measured by using the SBMs questionnaire, between day -10 and day 84 (daily), according to the assessment of the patient as a part of the patient's diary
8. Change in bowel habits is measured by using a questionnaire at day 13, day 27, day 55, day 83 (one day before scheduled visit), according to the assessment of the patient as a part of the patient's diary
9. The time point of the first perceived abdominal symptom improvement after randomisation is measured by using a questionnaire between day 0 and day 28 (daily), according to the assessment of the patient as a part of the patient's diary
10. Patient´s satisfaction with the randomized treatment is measured by using the Integrative Medicine Patient Satisfaction Scale (IMPSS) at day 13, day 27, (one day before scheduled visit), according to the assessment of the patient as a part of the patient's diary
11. The use of BUSCOPAN® PLUS film-coated tablets is documented between day 0 and day 84 (daily), according to the assessment of the patient as a part of the patient's diary
12. The tolerability is measured by using a 5-point Likert Scale at day 13, day 27, day 55, day 83 (one day before scheduled visit), according to the assessment of the patient as a part of the patient's diary as well as on day 14, day 28, day 56, and day 84, according to the assessment of the investigator

Completion date
31/03/2019

Eligibility

Key inclusion criteria
1. Aged 18 years and over
2. Provision of written informed consent in accordance with the legal requirements
3. Willing and able to comply with all study procedures
4. Diagnosis of irritable bowel syndrome (IBS) based on the following criteria:
4.1. Presence of IBS symptoms (e.g. abdominal pain, flatulence) for > 3 months
4.2. IBS symptoms are ascribed by both patient and physician to the gut and usually accompanied by altered bowel habits
4.3. The IBS complaints are the reason, why the subject consulted the physician
4.4. No changes characteristic of other diseases are present that are likely to be the cause of the symptoms
5. Numeric Rating Scale (NRS) assessing severity of pain > 3 points at visit 1 and visit 2, respectively
6. Any reduction in numeric pain rating scale (NRS) assessing severity of pain at visit 2 not greater than one point in comparison to visit 1
7. IBS-Severity Scoring System (IBS-SSS) > 80 points at visit 1 and 2, respectively
8. Any reduction in IBS-SSS at visit 2 in comparison to visit 1 is < 25 points

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
226

Key exclusion criteria
1. History of chronic or evident acute liver, heart, respiratory tract, pulmonary, muscular (e.g. M. gravis) or renal disease
2. History or suspected glaucoma (angel-closure glaucoma)
3. Subjects with a history of urinary retention by mechanical narrowing of the urinary tract (e.g. enlarged prostate)
4. History of renal or hepatic dysfunction (serum creatinine, serum AST or ALT at least 3 folds above the upper limit of normal range or alkaline phosphatase > 2 fold above the upper limit of normal) within the last 12 months prior to inclusion into the study

5. Subject with known or suspected gall bladder inflammation (cholangitis), is suffering from gall stone, occlusion of the bile ducts or other diseases of the gall bladder, sphincter Oddi dysfunction, or abdominal adhesions
6. History or suspected pancreatitis, ileus, or any gastrointestinal bleeding
7. Female subject suffering from endometriosis
8. Subject is immune-compromised (e.g. AIDS, lymphoma, long-term corticosteroid treatment)
9. Subject with malignant tumours or undergoing chemotherapy or radiation therapy
10. Evidence of structural abnormality of the gastrointestinal tract or diseases/conditions that affect bowel transit (e.g. mega-colon)
11. Subject is suffering from gastro-oesophageal reflux disease (GERD) or reduced production of gastric acid (achlorhydria)
12. Evident or suspected other causes for diarrhoea such microscopic colitis, celiac disease
13. Subject is currently experiencing nausea, fever > 38.5 °C (measured using an infrared ear thermometer), vomiting, or bloody diarrhoea
14. Subject with history of a gastrointestinal surgery (except appendectomy conducted before one year or longer)
15. Subject with clinically significant abnormal results of laboratory tests at the time point of visit 1 (including haematology tests, serum chemistry tests, thyroid function tests)
16. Subject is 50 years or older who has been diagnosed with IBS and has not received a colonoscopy in the last 6 months prior to inclusion into the study
17. Subject with history of positive test of blood in stool within the last 6 months prior to inclusion into the study
18. Subject with history of clinically relevant increase in stool calprotectin within the last 6 months prior to inclusion into the study
19. Subject using or has used antipsychotic, antidepressive or anticholinergic medication within one month prior to inclusion into the study
20. Previous (within the last 14 days) or concomitant use of analgesics, prokinetics, sedatives, laxatives, anti-diarrhoeal agents, steroidal agents, antacids, proton-pump inhibitors, anti-coagulants, antibiotics or probiotics
21. Known or suspected hypersensitivity to the investigational drug or to one of its excipients or to peppermint, menthol, caraway, or to umbelliferous plants or to the rescue medication (BUSCOPAN® PLUS) offered in the study or one of its excipients
22. Previous (within the last 30 days) or current use of medications for the treatment of IBS (including herbal preparations)
23. Women with positive pregnancy test at visit 1
24. Pregnant or breast-feeding women
25. Female subject is currently not using an acceptable form of birth control or does not agree to maintain its use throughout the study
26. Subject exhibiting or indicating thoughts of suicide currently or in the past
27. Subject with no willingness and no ability to comply with all procedures of the trial and is not able to attend all scheduled visits at the investigational site
28. Participation in a further clinical trial at the same time or within the last 3 months prior to inclusion into the present study
29. Previous randomisation in the present clinical study
30. Subject with known or suspected history of alcohol or drug abuse according to the opinion of the investigator
31. Subjects whose participation in the clinical trial results in an unjustifiable impairment of their well-being according to the opinion of the investigator
32. Planned surgical intervention during the clinical study

Date of first enrolment

11/07/2016

Date of final enrolment
04/09/2017

Locations

Countries of recruitment
Germany

Study participating centre
KRH Klinikum Siloah-Oststadt-Heidehaus
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Sponsor information

Organisation
Dr. Willmar Schwabe GmbH & Co. KG

ROR
https://ror.org/043rrkc78

Funder(s)

Funder type
Industry

Funder Name
Dr. Willmar Schwabe GmbH & Co. KG

Results and Publications

Individual participant data (IPD) sharing plan
The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			23/06/2020	No	No