

# 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)

<b>Submission date</b> 09/05/2016	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 17/05/2016	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 23/06/2020	<b>Condition category</b> Digestive System	<input type="checkbox"/> 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

KRH Klinikum Siloah-Oststadt-Heidehaus

Stadionbrücke 4

Hannover

Germany

30449

## Additional identifiers

### EudraCT/CTIS number

2014-004702-14

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers

530079.01.302

## Study information

### Scientific Title

Efficacy and tolerability of Menthacarin® in patients ( $\geq 18$  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

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Home

**Study type(s)**

Treatment

**Participant information sheet**

Not available in web format, please use the contact details below to request a patient information sheet.

**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  $\pm$  4 days after randomization

Visit 4: 28 days  $\pm$  4 days after randomization (End of double-blind treatment period)

Visit 5: 56 days  $\pm$  4 days after randomization (End of follow-up double-blind treatment period)

Visit 6: 84 days  $\pm$  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 measure**

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.

## **Secondary outcome measures**

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

**Overall study start date**

21/02/2014

**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

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

200

**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 (angle-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**

Stadionbrücke 4

Hannover

Germany

30449

**Study participating centre**

**Gemeinschaftspraxis für Allgemeinmedizin**

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**Study participating centre**

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**Studienzentrum Dr. med. Andreas Schwittay**  
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**Study participating centre**  
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**Study participating centre**  
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**Study participating centre**  
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22299

## Sponsor information

### Organisation

Dr. Willmar Schwabe GmbH & Co. KG

### Sponsor details

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76227

### Sponsor type

Industry

### ROR

<https://ror.org/043rrkc78>

## Funder(s)

### Funder type

Industry

### Funder Name

Dr. Willmar Schwabe GmbH & Co. KG

## Results and Publications

### Publication and dissemination plan

Planned publication in a high-impact peer reviewed journal.

### Intention to publish date

31/03/2020

### 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?
<a href="#">Basic results</a>			23/06/2020	No	No