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SYN-001 in the treatment of chronic idiopathic constipation

Submission date 23/10/2018	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 08/11/2018	**Overall study status** Completed	
Last Edited 20/01/2020	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
With a prevalence of up to 18%, chronic constipation is one of the most common health disorders in Germany. The prevalence increases with age and women are significantly more affected than men. Due to the high prevalence, this disease is responsible for significant healthcare costs. Chronic constipation is a persistent bowel disorder with irregular bowel movements, accompanied by various symptoms such as severe stool consistency, and pressure and pain during bowel movements. The numerous symptoms of chronic constipation are often associated with a high degree of suffering, and in some cases they affect the patient's quality of life significantly.
Associations between constipation and a low-fiber diet, reduced fluid intake, lack of exercise and suppression of defecation and abrupt lifestyle changes have been found. Current therapies for chronic constipation are limited to the treatment of constipation itself and do not take into account possible accompanying symptoms. A treatment approach that increases the number of bowel movements and improves possible unpleasant symptoms of constipation (such as flatulence, bloating and associated abdominal pain) at the same time, while being safe and well-tolerated, is highly beneficial for the patient.
The aim of this study is to investigate the efficacy of the combination product SYN-001.

Who can participate?
Patients with chronic idiopathic constipation, aged between 18 and 80.

What does the study involve?
Each patient participates for 6 weeks in the trial. The first 2 weeks are a screening period to include appropriate patients, and the next 4 weeks are the treatment period. After the screening period, patients are randomly assigned to receive either SYN-001 (treatment group) or a placebo (control group) during the treatment period. In both groups, 3 portions are taken orally, daily for 4 weeks. For the preparation of one portion one measuring spoon of the granulate is to be stirred into 150-200 ml of water and consumed directly afterwards. One portion is consumed in the morning, the second portion at noon and the third portion in the evening.
During the 6 weeks each participant will visit the physician 3 times. During these visits physical examinations will be performed and vital signs will be determined. Further, a pregnancy test is

performed on female patients of childbearing age. Each patient must keep a daily diary detailing his/her symptoms over the whole study period.

What are the possible benefits and risks of participating?
For participating patients receiving SYN-001, constipation and related symptoms may be relieved. The results of this study may also help to improve the treatment of chronic constipation in the future.
Both methylcellulose and simethicone (the ingredients of SYN-001) are generally regarded as safe.
Participants in the control group may not receive any relief from constipation or related symptoms. However, if no bowel movement has occurred over more than 3 days, participants may use a laxative.
Therefore, there are no known risks to participants taking part in this study.

Where is the study run from?
The study is run from the medical centre of Dr. med. Manuela Thinesse-Mallwitz and 3 other medical centres in Germany

When is study starting and how long is it expected to run for?
March 2018 to January 2019

Who is funding the study?
Synformulas GmbH (Germany)

Who is the main contact?
Sonja Henneberger
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Study website
http://www.studie-verstopfung.de/

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Randomised, double-blind, placebo-controlled, multicentre trial for investigation of SYN-001 in the treatment of patients with chronic idiopathic constipation

Acronym
SYN-C-001

Study objectives
The combined responder rate is greater after consumption of SYN-001 than after consumption of placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethik-Kommission der Bayerischen Landesärztekammer (Ethics Commission of the Bavarian Local Medical Association), 15/05/2018, 18021

Study design
Interventional multi-centre double-blind randomised placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

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
Chronic idiopathic constipation

Interventions

Participants are randomised using block randomisation in a 1:1 ratio to either the treatment group or the control group. The treatment group will receive 3 portions of SYN-001 (with Synformularis2 Faserkomplex (containing methylcellulose) and simethicone - 2 g methylcellulose and 0.125 g simethicone per portion) per day for 4 weeks. The control group will receive 3 portions of placebo per day for 4 weeks.
The trial consists of 2 periods - a 2 week run-in period followed by a 4 week treatment period. There will be 3 visits to the physician per participant:
1. Visit 1 - prior to the run-in phase
2. Visit 2 - after the run-in phase and before the treatment phase
3. Visit 3 - after the treatment phase

Intervention Type
Other

Primary outcome measure
Response rate, based on complete spontaneous bowel movements (CSBMs) per week, assessed using a patient diary (using the question "How many CSBMs have you had within the last 24 hours?") on a daily basis

Secondary outcome measures
The following are assessed using a patient diary:
1. Frequency of CSBMs, assessed using the question "How many CSBMs have you had within the last 24 hours?" on a daily basis for the study duration
2. Stool consistency, assessed using the Bristol Stool Form Scale (BSFS) on a daily basis for the study duration
3. Pain during defecation, straining during defecation, sensation of bloating and flatulence, assessed using a 5-point Likert scale on a daily basis for the study duration
4. Number of symptom-free days, assessed on a daily basis for the study duration
5. Subjective assessment of weight change, assessed using a 5-point Likert scale on a weekly basis for the study duration
6. Use of emergency medication (Bisacodyl suppositories), assessed on a daily basis for the study duration
7. Satisfaction of bowel function, assessed using a 5-point Likert scale on a weekly basis for the study duration
8. Suffering from constipation, sensation of bloating and flatulence, assessed using a 5-point Likert scale on a weekly basis for the study duration
9. Adequate relief and adequate relief responder, assessed using a 5-point Likert scale on a weekly basis for the study duration

The following are assessed using a questionnaire at the physician visits:
10. Subjective assessment by patients and physician of efficacy of treatment, assessed using a 5-point Likert scale at visit 3
11. Quality of life, assessed using the Patient Assessment of Constipation Quality of Life questionnaire (PAC-QoL) at visit 2 (after the run-in phase and before the treatment phase) and visit 3 (after the treatment phase)
12. Weight change, assessed using a weighing scale at visits 1, 2 and 3
13. Abdominal girth change, assessed using a measuring tape at visits 1, 2 and 3
14. Tolerance and safety, assessed using a 5-point Likert scale at visit 3

Overall study start date
01/03/2018

Completion date
31/01/2020

Eligibility

Key inclusion criteria
1. Patients with chronic idiopathic constipation according to current EMA-Guideline:
1.1. A patient must fulfil 2 or more of the following 3 criteria:
1.1.1. Fewer than 3 defecations per week
1.1.2. Straining during at least 25% of defecations
1.1.3. Lumpy or hard stools in at least 25% of defecations
1.2. A patient must fulfil all of the following:
1.2.1. Loose stools (type 6 or 7 on the Bristol Stool Scale) are rarely present without the use of laxatives at visit 1 and occurs during the run-in period on less than 3 days
1.2.2. No defecation disorders
1.2.3. Insufficient criteria for irritable bowel syndrome according to the Rome III criteria
1.2.4. No other causes are identifiable for constipation (e.g. medication)
These criteria should be fulfilled at recruitment (by history taking), and during the run-in period of the studies.
In addition to that, during the Run-In period, the number of stools should not exceed 5 in two weeks.
2. Otherwise healthy
3. Aged 18-80 years
4. Negative result of a sigmoidoscopy or colonoscopy within the preceding 5 years for patients above 55 years of age
5. Legal capacity
6. Written consent of the patient
7. Understanding of the German language and compliance
8. Understanding that changes in lifestyle and nutrition habits have to be avoided
9. Understanding the principle of the patient diary and is willing to keep it according to the requirements
10. Negative pregnancy test in women capable of bearing children

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
80 Years

Sex
Both

Target number of participants
204

Key exclusion criteria

1. Hypersensitivity towards the study product or Bisacodyl
2. New symptoms during the last weeks, such as anemia, rectal bleeding, positive fecal occult blood test or severe weight loss
3. Secondary reasons for constipation:
3.1. Intake of medicaments (e.g. opioids, tricyclic antidepressants, duretics)
3.2. Organic/metabolic/neurological diseases (e.g. hypercalcemia, anemia, dementia, collagenosis, Parkinson's disease, multiple sclerosis, Hirschsprung's disease)
3.3. Bowel dysfunction (e.g. structural intestinal passage disorder, bowel obstruction, slow-transit-constipation, intestinal stenosis)
3.4. Eating disorders (e.g. anorexia, bulimia)
3.5. Physical inactivity
3.6. Eating disorder
4. Fluid intake of <0.5 l of fluid per day
5. Inadequate response to usual laxatives (psyllium, sauerkraut juice, Dulcolax, Lefax, Lacoberal, Bisacodyl)
6. Inflammatory bowel diseases (Crohn's disease and Ulcerative colitis)
7. Systemic diseases, cancer, autoimmune diseases
8. Known abnormalities in abdomen region e.g. unusual ultrasound that would require further investigation
9. Ileus, bowel obstruction or acute surgical conditions
10. Defecation disorders
11. Irritable bowel syndrome
12. Surgical intervention within the next 3 months
13. Current cancer diagnosis or cancer within the last 5 years or any colorectal cancer diagnosis
14. Ingestion of any of the following:
14.1. Opioids within the last 6 months prior to study start
14.2. Antipsychotics/antideperessants within the last 3 months prior to study start
14.3. Antibiotics within the last 2 months prior to study star
14.4. Systemic corticosteroids within the last month prior to study start
14.5. Medications that may affect the efficacy of the study product (e.g. analgesics, antibiotics, chemotherapeutics, psychotropics/antidepressants, laxatives, spasmolytics, antidiarrhoeals, probiotic products)
15. Serious psychiatric disorders within the last 2 years
16. Diabetes mellitus
17. Hyperthyroidism and non-set hypothyroidism
18. Immune deficiency
19. Abdominal surgeries (exceptions include: appendectomies, hernia surgeries, cholecystectomy and sectio caesarea if undertaken more than 6 months prior to study start)
20. Coeliac disease
21. Fever
22. Known parasites or eggs in stool
23. Serious diseases resulting in a need for care, a need for a guardian or resulting in immobilisation
24. Gynecological diseases
25. Alcohol or drug abuse
26. Pregnancy or lactation period
27. Participation in other interventional trials or participation in other interventional trials within the last 30 days
28. Nonautonomous individuals, not capable of making decisions independently e.g. due to a relationship with a sponsoring party or relationship with a physician, both of whom may be

capable of pressuring the participant
29. Accommodation in an asylum due to court or administrative order

Date of first enrolment
29/06/2018

Date of final enrolment
20/12/2019

Locations

Countries of recruitment
Germany

Study participating centre
Medical practice Dr. med. Manuela Thinesse-Mallwitz (lead centre)
Fäustlestraße 3
Munich
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80339

Study participating centre
Medical practice Dr. med. Guntram Bloß
Aribonenstraße 15
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Study participating centre
Medical practice Dr. med. Ralph Czekalla
Rosenheimer Str. 52
Munich
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Study participating centre
Medical practice Dr. med. Manuela Nader
Tulpenstraße 26
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82110

Sponsor information

Organisation
Synformulas GmbH

Sponsor details
Am Haag 14
Gräfelfing
Germany
82166

Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Synformulas GmbH

Results and Publications

Publication and dissemination plan
A manuscript including the data of the trial is intended to be published in 2019.

Intention to publish date
31/05/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to data protection.

IPD sharing plan summary
Not expected to be made available