# SYN-001 in the treatment of chronic idiopathic constipation

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

#### 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
s.henneberger@fgp-pharma.de

#### Study website

http://www.studie-verstopfung.de/

# **Contact information**

# Type(s)

**Public** 

#### Contact name

Ms Sonja Henneberger

#### Contact details

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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 Germany 80339

#### Study participating centre Medical practice Dr. med. Guntram Bloß

Aribonenstraße 15 Munich Germany 81669

# Study participating centre Medical practice Dr. med. Ralph Czekalla

Rosenheimer Str. 52 Munich Germany 81669

# Study participating centre Medical practice Dr. med. Manuela Nader

Tulpenstraße 26 Germering Germany 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