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Clinical trial for proving the efficacy of heat-inactivated Bifidobacterium bifidum SYN-HI-001 in the treatment of irritable bowel syndrome

Submission date
08/04/2016

Recruitment status
No longer recruiting

Registration date
11/04/2016

Overall study status
Completed

Last Edited
15/04/2020

Condition category
Digestive System

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

Plain English summary of protocol

Current plain English summary as of 05/08/2019:
Background and study aims
Irritable bowel syndrome (IBS) is one of the most common disorders of the digestive system in the European population. IBS is part of a group of diseases called functional bowel disorders, and is associated with various symptoms such as abdominal pain, diarrhea, constipation and flatulence. Current treatments are limited to treating these symptoms and so far there is no single therapy used to treat patients. Many of the existing drug therapies are associated with significant side effects. Several studies have stated that in people with IBS, the barrier function of the intestine is compromised, allowing bacteria to pass through it and into the inner most layers of the bowel wall (intestinal mucosa) due to increased intestinal permeability. This movement of bacteria (bacterial translocation) is thought to be responsible for IBS symptoms. Bifidobacteria can stick to cells lining the intestine in groups, forming a natural coating (biofilm). This biofilm can help to improve the barrier function of the intestine, and help alleviating IBS symptoms or induction of remission. Based on the demonstrated in vitro adhesive behavior of heat-inactivated Bifidobacteria bifidum (B. bifidum) to intestinal epithelial cells, the aim of this study is to find out whether taking heat-inactivated B. bifidum SYN-HI-001 is an effective and safe treatment for IBS.

Who can participate?
Adults with IBS.

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in the first group take two capsules a day at mealtimes containing heat-inactivated B. bifidum SYN-HI-001 for eight weeks. Participants in the second group take two placebo (dummy) capsules a day at mealtimes for eight weeks. Participants in both groups attend study visits at the physician two weeks before treatment, at the start of treatment, after four weeks of treatment, after eight weeks of treatment and two weeks after the end of treatment. During these visits, participants have a

physical examination (at each visit) and blood samples are collected (at the beginning and at the end of the study). In addition, participants must keep a daily diary at home detailing his/her symptoms over the whole study period.

What are the possible benefits and risks of participating?
Participants taking B. bifidum SYN-HI-001 may benefit from an improvement of their IBS symptoms and quality of life via a safe treatment. Bifidobacteria are generally regarded as safe and in Europe they possess the QPS (qualified presumption of safety) status by the EFSA (European Food Safety Authority) and in the US the GRAS (Generally Recognized as Safe)-status. In addition, the incidence of adverse events in clinical trials with Bifidobacteria is comparable to placebo. The bacteria contained in the test product (B. bifidum SYN-HI-001) were isolated from a fecal sample of a healthy person. In addition, the strain is heat inactivated. However, this process does not lead to a release of cell fragments nor does it affect the morphological form of the bacterial cells. Therefore, it can be assumed that the rate of adverse events is no different from ingesting the living bacterial strain. Thus, the risks of this trial are equal to those conventionally associated with ingesting commercial probiotic products, which are considered to be low. Over the course of the blood sampling the usual side effects of blood sampling can occur.

Where is the study run from?
Israelite Hospital in Hamburg (lead centre) and about 25 medical centres in Hamburg and Munich (Germany)

When is study starting and how long is it expected to run for?
September 2015 to December 2016

Who is funding the study?
Synformulas GmbH (Germany)

Who is the main contact?
1. Sonja Henneberger (public)
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2. Bastian Baasch (scientific)
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Previous plain English summary:
Background and study aims
Irritable bowel syndrome (IBS) is one of the most common disorders of the digestive system in the European population. IBS is part of a group of diseases called functional bowel disorders, and is associated with various symptoms such as abdominal pain, diarrhea, constipation and flatulence. Current treatments are limited to treating these symptoms and so far there is no single therapy used to treat patients. Many of the existing drug therapies are associated with significant side effects. Several studies have stated that in people with IBS, the barrier function of the intestine is compromised, allowing bacteria to pass through it and into the inner most layers of the bowel wall (intestinal mucosa) due to increased intestinal permeability. This movement of bacteria (bacterial translocation) is thought to be responsible for IBS symptoms. Bifidobacteria can stick to cells lining the intestine in groups, forming a natural coating (biofilm). This biofilm can help to improve the barrier function of the intestine, and help alleviating IBS symptoms or induction of remission. Based on the demonstrated in vitro adhesive behavior of heat-inactivated Bifidobacteria bifidum (B. bifidum) to intestinal epithelial cells, the aim of this study is to find out whether taking heat-inactivated B. bifidum FGP-IBS-HI007 is an effective and safe treatment for IBS.

Who can participate?
Adults with IBS.

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in the first group take two capsules a day at mealtimes containing heat-inactivated B. bifidum FGP-IBS-HI007 for eight weeks. Participants in the second group take two placebo (dummy) capsules a day at mealtimes for eight weeks. Participants in both groups attend study visits at the physician two weeks before treatment, at the start of treatment, after four weeks of treatment, after eight weeks of treatment and two weeks after the end of treatment. During these visits, participants have a physical examination (at each visit) and blood samples are collected (at the beginning and at the end of the study). In addition, participants must keep a daily diary at home detailing his/her symptoms over the whole study period.

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September 2015 to December 2016

Who is funding the study?
PharmaFGP GmbH (Germany)

Who is the main contact?
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Contact information

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Study information

Scientific Title
Randomised, double-blind, placebo-controlled, multicentre clinical trial for proving the efficacy of heat-inactivated Bifidobacterium bifidum SYN-HI-001 in the treatment of patients with irritable bowel syndrome

Acronym
SYN-HI-001

Study objectives
Current study hypothesis as of 05/08/2019:
The combined responder rate is greater after consumption of SYN-HI-001 than after consumption of placebo.

Previous study hypothesis:
The combined responder rate is greater after consumption of FGP-IBS-HI007 than after consumption of placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)

Ärztekammer Hamburg (Medical Association Hamburg), 18/01/2016 (advisory opinion), ref: PV5163

Study design
Multicentre randomised double-blind placebo-controlled clinical trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Current interventions as of 05/08/2019:
Participants are block randomised into two groups in a 1:1 ratio.

Treatment group: Participants take two capsules containing heat-inactivated B. bifidum SYN-HI-001 (0,5x10^9 cfu per capsule) per day for 8 weeks.
Control group: Participants take two placebo capsules per day for 8 weeks.

The trial consists of three phases:
1. Run-in phase (2 weeks)
2. Treatment phase (8 weeks)
3. Wash-out phase (2 weeks)

The trial includes five visits per participant at the physician:
1. Before run-in phase (visit 1)
2. After run-in phase and before treatment phase (visit 2)
3. Middle of treatment phase (after 4 weeks of treatment) (visit 3)
4. After treatment phase and before wash out phase (visit 4)
5. After wash-out phase (visit 5)

Previous interventions:
Participants are block randomised into two groups in a 1:1 ratio.

Treatment group: Participants take two capsules containing heat-inactivated B. bifidum FGP-IBS-HI007 (0,5x10^9 cfu per capsule) per day for 8 weeks.
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3. Middle of treatment phase (after 4 weeks of treatment) (visit 3)

4. After treatment phase and before wash out phase (visit 4)
5. After wash-out phase (visit 5)

Intervention Type
Other

Primary outcome(s)
Response-rate based on adequate relief of IBS symptoms in combination with an improvement in abdominal pain at the end of the treatment phase, adequate relief of IBS symptoms is measured weekly for 10 weeks (during the treatment phase and the wash out phase) using the 7-point Likert scale, abdominal pain is measured daily for 12 weeks using the 11-point numerical rating scale (NRS).

Key secondary outcome(s)
Current secondary outcome measures as of 14/08/2019:
1. Response-rates of the single parameters of the combined endpoint, adequate relief of IBS symptoms is measured weekly for 10 weeks (during the treatment phase and the wash out phase) using the 7-point Likert scale, abdominal pain is measured daily for 12 weeks using the 11-point numerical rating scale (NRS).
2. Change in Mental Health Sum is measured using the SF-12 health survey at baseline and at the end of treatment.

Previous secondary outcome measures:
1. Response-rates of the single parameters of the combined endpoint, adequate relief of IBS symptoms is measured weekly for 10 weeks (during the treatment phase and the wash out phase) using the 7-point Likert scale, abdominal pain is measured daily for 12 weeks using the 11-point numerical rating scale (NRS)
2. Subject’s global assessment of symptoms, measured daily for 12 weeks using the 7-point Likert scale
3. Spontaneous bowel movements (numerically), stool consistency (using the Bristol Stool Form Scale), and feeling of incomplete evacuation (numerically), measured daily for 12 weeks
4. Mucus and blood in stool, measured numerically on a weekly basis for 12 weeks
5. Symptom-free and pain-free days, assessed daily for 12 weeks using the 7-point Likert scale of the subject’s global assessment of symptoms and the 11-point numerical rating scale of abdominal pain measurement
6. Severity of IBS symptoms, measured at visits 2, 3, 4 and 5 using the IBS-severity symptom system (IBS-SSS) score
7. Quality of life, measured at visits 2, 3 and 4 using the SF-12 health survey
8. Safety, using results of vital parameters (measured at visits 1, 2, 3, 4 and 5), blood samples (collected at visits 1 and 5), adverse events (assessed at visits 1, 2, 3, 4 and 5) and subjective assessment of tolerability of the test product via the patient (assessed at visits 3, 4 and 5)

Completion date
15/04/2017

Eligibility

Key inclusion criteria
1. Patients with IBS, diagnosed according to the Rome-III-criteria
2. Otherwise healthy male or female subjects, aged between 18 and 65 years
3. Negative result of a sigmoidoscopy or coloscopy within the preceding 5 years for patients

above 55 years of age
4. Legal capacity
5. Written consent of the patient
6. Understanding of the German language and compliance
7. Patient has understood, that changes in life style and nutrition habits have to be avoided
8. Patient has understood the principle of the patient-diary and is willing to keep it according to the requirements
9. Negative pregnancy test

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
507

Key exclusion criteria
1. Inflammatory bowel diseases (Crohn's disease and Ulcerative colitis)
2. Systemic diseases, cancer, autoimmune diseases
3. Known abnormalities in abdomen region e.g. unusual ultrasound that would require further investigation
4. Ingestion of antipsychotics within the last 3 months prior to the start of the study. Ingestion of systemic Corticosteroids wihtin the last month prior to the start of the study.
5. Ingestion of medication influencing the efficacy of the tested product (i.e. analgetics, antibiotics, chemotherapeutics, antipsychotics, laxatives, spasmolytics, antidiarrhoeals)
6. Ingestion of other probiotic products
7. Serious psychiatric disorders within the last 2 years
8. Diabetes mellitus
9. Hyperthyroidism and hypothyroidism
10. Lactose intolerance or other malabsorption syndromes
11. Immune deficiency
12. Abdominal surgeries (exceptions include: appendectomies, hernia surgeries, cholecystectomy, sectio caesarea)
13. Coeliac disease
14. Known positive stool culture for patients with diarrhea-predominant IBS
15. Fever
16. Known parasites or eggs in stool
17. Laboratory abnormalities which would expose the patient to an unacceptable risk or influence intepretation of study data
18. Serious diseases resulting in a need for care, a need for a guardian or resulting in

immobilisation
19. Alcohol or drug abuse
20. Pregnancy or lactation period
21. Participation in other interventional trials or participation in other interventional trials within the last 30 days
22. 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

Date of first enrolment
20/04/2016

Date of final enrolment
15/01/2017

Locations

Countries of recruitment
Germany

Study participating centre
Isrealite Hospital Hamburg
Hamburg
Germany
22297

Sponsor information

Organisation
Synformulas GmbH

Funder(s)

Funder type
Industry

Funder Name
Synformulas GmbH

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/07/2020	15/04/2020	Yes	No
Basic results		12/08/2019	14/08/2019	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes