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# RM-001, a new combinational product of digestive enzymes and gastric acid regulator, for the treatment of upset stomach (functional dyspepsia) and related symptoms

**Submission date**
15/05/2019

**Recruitment status**
No longer recruiting

**Registration date**
01/07/2019

**Overall study status**
Completed

**Last Edited**
22/12/2020

**Condition category**
Digestive System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

## Plain English summary of protocol

Background and study aims
With a prevalence of up to 15%, upset stomach (functional dyspepsia) is one of the most common functional gastrointestinal disorders worldwide. However, the number of patients with upset stomach and related symptoms without consulting a doctor is much higher, approximately a quarter of the population. Although differences between the genders could not be demonstrated in most population-based studies, some publications indicate that women are more likely to be affected by functional dyspepsia than men.
The symptoms of upset stomach are related to the upper abdomen which occur recurrently and in some cases significantly impair the quality of life of those affected. Typical symptoms include postprandial fullness, early satiation, belching, heartburn, stomach cramps, nausea and pain and burning in the upper abdominal or stomach area. The complaints often occur postprandial (after a meal), but can also occur regardless of food intake.
From a pathophysiological point of view, it was possible to detect disturbed gastric motility and disproportionate volume distribution in the stomach in connection with delayed gastric emptying in patients with upset stomach. The increased intragastric pressure and the increased gastric wall tension lead to symptoms such as a feeling of fullness, early satiation, nausea and belching. In addition, stomach and intestinal wall (in the area of the duodenum) of patients with upset stomach show increased sensitivity to gastric acidity. As a result, patients suffer from pain and burning in the stomach area.
There is no standard therapy for the treatment of upset stomach. The AkdÄ (Arzneimittelkommission der deutschen Ärzteschaft) recommends as a first-line drug therapy proton pump inhibitors (PPIs) or subordinate H2 receptor antagonists to reduce gastric acid production. Due to uncertain data and adverse effects, prokinetic agents are considered as second-line drug therapy and are used in patient with symptoms related to motility. All of these drug groups are associated with significant side effects.
More tolerable alternatives for the treatment of upset stomach are enzymes and antacids (e.g. natural minerals) which have been available on the market for decades as nutritional supplements or medical devices. The efficacy and safety was tested and confirmed in preclinical

and clinical studies as well as in everyday clinical practice. The aim of the present study is to further investigate a new product (RM-001) consisting of a combination of fungal enzymes (protease, lipase) and an antacid (calcium carbonate) in patients with upset stomach (functional dyspepsia) and related symptoms, which has been specifically developed for the motility-related and acid-related symptoms of upset stomach.

Who can participate?
Male and female patients with upset stomach (functional dyspepsia) and the related symptoms, aged between 18 and 80.

What does the study involve?
Each patient participates for 5 weeks in the trial. The first week is 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 RM-001 (treatment group) or a placebo (control group) during the treatment period. In both groups, 3 capsules are taken orally, daily for 4 weeks. Each capsule is consumed directly after a meal.
During the 5 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 RM-001, upset stomach and related symptoms may be relieved. The results of this study may also help to improve the treatment of upset stomach (functional dyspepsia) in the future. All ingredients of RM-001 (lipase, protease and calcium carbonate) are generally regarded as safe. For similar enzyme preparations, in rare cases (1 - 10 out of 10,000) unspecific side effects such as diarrhea, nausea, constipation and upper abdominal complaints have been observed. After occupational sensitization with mould enzymes allergic respiratory and skin reactions have been reported. For the investigational combination product RM-001, no side effects have been observed so far.
Participants in the control group may not receive any relief from upset stomach and related symptoms. However, in case of emergency (with long-lasting and very severe intensity of symptoms), the patient may use medication according to current recommendations of guidelines after consultation with the investigator. The use of these drugs must be documented in the diary and CRF.
The benefit-risk assessment concludes, that the possible benefits clearly outweigh risks.

Where is the study run from?
The study is run from the medical centre of Dr. med. Denise F. Eder (leading physician) and other medical centres in Germany. If necessary, more qualified centres can be included.

When is study starting and how long is it expected to run for?
August 2018 - July 2019, with an estimated recruiting period of circa 5-6 months.

Who is funding the study?
Synformulas GmbH (Gräfelfing, Germany)

Who is the main contact?
Sonja Henneberger (S.Henneberger@fgp-pharma.de)

# Contact information

### Type(s)
Public

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## Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### ClinicalTrials.gov (NCT)
Nil known

### Protocol serial number
Nil known

## Study information

### Scientific Title
Investigation of RM-001 in a double-blind, placebo-controlled, multicenter study in patients with upset stomach (functional dyspepsia) and related symptoms

### Acronym
SYN-RM-001

### Study objectives
The Adequate Relief Response rate is greater after consumption of RM-001 than after consumption of placebo.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approved 14/12/2018, Ethik-Kommission bei der Landesärztekammer Hessen (ethics commission of the local medical association Hesse, Im Vogelsgesang 3, 60488 Frankfurt am Main, Germany; +49(0)69 97672-209 ext.119; ethikkommission@laekh.de), ref: FF 116/2018

### 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
Upset stomach (functional dyspepsia) and related symptoms

## Interventions
Treatment: 3 capsules (Lipase, Protease and antacid) of RM-001 per day for 4 weeks
Control: 3 capsules of placebo per day for 4 weeks
Randomisation: 1:1 randomisation in blocks

The trial consists of two periods:
1. Run-in period (1 week)
2. Treatment period (4 weeks)

The trial includes three 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. After treatment phase (visit 3)

Data are gathered on paper-based CRFs (patient diaries and questionnaires filled in by the physician).

## Intervention Type
Other

## Primary outcome(s)
Adequate Relief Response, defined as reaching one of the best 3 categories on a 5 point Likert scale, assessed using the question "How would you assess the relief of your disease compared to before taking the test product?" on a weekly basis for the study duration.

## Key secondary outcome(s))
The following are assessed using a patient diary:
1. Adequate Relief, assessed using a 5-point Likert scale on a weekly basis for the study duration
2. Overall Symptom Score (including assessment of postprandial fullness, early satiation, gastric pain, gastric burning, heart burn, belching, nausea, gastric cramps, bloating and flatulence), assessed using a 5-point Likert scale on a daily basis for the study duration
3. Individual symptoms of the Overall Symptom Score, assessed using a 5-point Likert scale on a daily basis for the study duration
4. Suffering by the single symptoms gastric pain, postprandial fullness, gastric burning and nausea, assessed using a 5-point Likert scale on a weekly basis for the study duration
5. Suffering by the totality of all symptoms, assessed using a 5-point Likert scale on a weekly basis for the study duration
6. Satisfaction with stomach activity, assessed using a 5-point Likert scale on a weekly basis for the study duration
7. Duration until onset of efficacy, assessed using a 5-point Likert scale on a daily basis for the study duration
8. Symptom Global Assessment (SGA), assessed using a 5-point Likert scale on a weekly basis for

the study duration
9. Combination of Adequate Relief and Overall Symptom Score, assessed as described under 1. and 2.

The following are assessed using a questionnaire at the physician visits:
10. Health-related quality of life, assessed using the SF-12 questionnaire at visit 2 (after the run-in phase and before the treatment phase) and visit 3 (after the treatment phase)
11. Efficacy of treatment assessed by patients and physician, assessed using a 5-point Likert scale at visit 3
12. Adequate Relief, assessed using a 5-point Likert scale at visit 3
13. Tolerance and safety assessed objectively by patients and physician, assessed using a 5-point Likert scale at visit 3
14. Tolerance and safety assessed by occurence of adverse events at visits 2 and 3 and measurement of vital parameters (body weight, abdominal girth, blood pressure, pulse and body temperature) using a body scale, a measuring tape and a sphygmomanometer at visits 1, 2 and 3

### Completion date
31/07/2019

## Eligibility

### Key inclusion criteria
1. Patients with upset stomach (functional dyspepsia) and related symptoms. A patient must fulfil the following:
1.1 One or more of the following symptoms occurs on at least 3 days per week with at least moderate intensity:
- postprandial fullness
- early satiation
- gastric pain
- gastric burning
1.2 Fulfillment of symptom criteria at recruitment (by history taking), and during the Run-in period of the study with onset of the symptoms more than 6 months prior to study start.
1.3 Presence of a malignant disease, which causes the dyspeptic symptoms, is to be excluded by the investigator on the basis of the current medical history and preliminary findings
2. Aged 18-80 years
3. Capacity for consent
4. Written informed consent of the patient
5. Understanding of the German language and compliance
6. Patient has understood, that changes in lifestyle and nutrition habits have to be avoided
7. Patient has understood the principle of the patient-diary and is willing to keep it according to the requirements
8. Negative pregnancy test in women capable of bearing children

### Participant type(s)
Patient

### Healthy volunteers allowed
No

### Age group
Adult

## Lower age limit
18 years

## Upper age limit
80 years

## Sex
All

## Key exclusion criteria
1. Hypersensitivity towards enzymes or allergy to mould
2. Familial predisposition (first degree) with GI carcinoma if the presence of carcinoma has not been excluded by gastroscopy within the last 5 years
3. Acute or recurrent occurence of alarm symptoms (anemia, unintentional weight loss (>10% of body weight), fever, lymph node enlargement, hematemesis, vomiting, melena)
4. Organic diseases: esophagitis, GERD, Barrett's esophagus, gastritis, pancreatitis, exocrine pancreatic insufficiency
5. Other diseases: diabetes, chronic inflammatory bowel disease, diverticulitis, liver disease, disease of the genitourinary system, cholecystitis and presence of gallstones, dysphagia, odynophagia, ulcus in the digestive tract, malabsorption
6. Infectious and parasitic causes and acute infections and parasitic infection
7. Systemic diseases, current cancer diagnosis or cancer within the last 5 years or any cancer diagnosis of the upper digestive tract (esophagus, stomach, duodenum), autoimmune diseases
8. Hyperthyroidism and unstable hypothyroidism
9. Hypercalcemia, hypercalciuria, kidney stones or calcification of the kidney
10. Food intolerances, celiac disease
11. Current pathological abdominal palpation or ultrasound findings
12. Abdominal surgeries (exceptions include: appendectomies, hernia surgeries, cholecystectomy and sectio caesarea if undertaken more than 6 months prior to study start)
13. Psychiatric or eating disorders within the last 2 years
14. Medications that may affect the efficacy of the study product (e.g. prokinetics, proton pump inhibitors, H2 receptor antagonists, phytotherapeutics, antidepressants or psychotropic drugs (no use within the last 3 months), antibiotics (no intake within the last 2 months), systemic corticosteroids (no use within the last month), chronic use of NSAID (except ASA 100 mg as a blood thinner), thiazide-type diuretics, cardiac glycosides)
15. Predominant symptoms of irritable bowel syndrome (patient primarily suffering from defecation disorders such as diarrhea or constipation)
16. Predominant symptoms of reflux oesophagitis (patient primarily suffering from heartburn)
17. Pregnancy or lactation period
18. A need for care, guardian or immobilisation
19. Alcohol or drug abuse
20. Participation in other interventional trials or participation in other interventional trials within the last 30 days
21. 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 putting pressure on the participant
22. Accommodation in an asylum due to court or administrative order

## Date of first enrolment
17/12/2018

**Date of final enrolment**
15/06/2019

# Locations

**Countries of recruitment**
Germany

**Study participating centre**
**Medical practice Dr. med. Denise F. Eder (lead centre)**
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**Study participating centre**
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**Study participating centre**
**Medical practice Dr. med. Ralph Czekalla**
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**Study participating centre**
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# Sponsor information

**Organisation**

Synformulas GmbH

# Funder(s)

**Funder type**
Industry

**Funder Name**
Synformulas GmbH

# Results and Publications

**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 reasons of data protection.

**IPD sharing plan summary**
Not expected to be made available

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |