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Next-generation probiotics for metabolic health

Submission date
18/11/2024

Recruitment status
No longer recruiting

Registration date
25/11/2024

Overall study status
Completed

Last Edited
30/10/2026

Condition category
Other

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

Plain English summary of protocol

Background and study aims
Probiotics are defined as “live microorganisms that, when administered in adequate amounts, confer a health benefit on the host”. Our gastrointestinal tract and the gut microbiota contain trillions of bacteria, which are important for functions such as digesting food and educating and activating the immune system. Next-generation probiotics (NGPs) are a completely new class of probiotics based on bacterial strains that naturally live in the human body. In this study, a potential NGP Akkermansia strain will be clinically tested for the first time in healthy volunteers.

Who can participate?
Healthy volunteers with no known medical conditions. The study will be run in the UK only at two private sites in Preston and Rochdale.

What does the study involve?
Participants will be invited to take part in this research study which is being conducted in one centre (with two locations) in the UK. It is planned that a total of up to 60 volunteers will be enrolled in the study and will be recruited within 2 months. Participants will be randomly assigned to one of three groups: (i) a low dose of the probiotic, (ii) a medium dose of the probiotic, (iii) a high dose of the probiotic, or (iiii) a product with no active probiotic (also known as a placebo). This study is a ‘double-blind’ study, which means that neither the participant nor the study doctor will know which group participants have been assigned to.

Participants will undergo a screening period of up to 2 weeks, they will take the active product or placebo for a period of 4 weeks and there will be a follow-up period of 4 weeks. The whole study is expected to take approximately 6 months.

This research study will use information from the participant (such as questionnaires) and their medical records. Blood, urine and faecal samples will also be taken during the study to check if the potential new probiotic is safe.

What are the possible benefits and risks of participating?
Prior to this study, some safety tests (known as toxicology assessments) were carried out on this potential probiotic and no significant issues were identified. However, as this product has not yet been tested in a clinical setting, it may have side effects that are unknown at the moment, and this study will look closely at any side effects participants may experience. However,

common temporary side effects of taking probiotics in general may include bloating, gas or mild flatulence. Some people may experience an allergic reaction if they are allergic to ingredients included in the study product.

Based on the nature of this trial, which will extend the understanding of the safety and tolerability of consuming a new Akkermansia strain in healthy adults there is no immediate benefits associated with this trial for the participants. However, participants will receive a general health assessment and blood and urine assessments and will receive information about their dietary habits and physical exercise levels, which may be of some interest or benefit. Should the study uncover anything about a participant's health, they will be informed by the study doctor.

Where is the study run from?
Danisco Sweeteners Oy (Finland)

When is the study starting and how long is it expected to run for?
May 2024 to October 2025

Who is funding the study?
Danisco Sweeteners Oy (Finland)

Who is the main contact?
Kasia Wzietal, kasia.wzietal@fgk-cro.com

Contact information

Type(s)
Public

Contact name
None Kasia Wzietal

Contact details
The Annexe, Saxon House, 28 Castle Street
Guildford
United Kingdom
GU1 3UW
+44 (0)1483 983404
kasia.wzietal@fgk-cro.com

Type(s)
Scientific

Contact name
Ms Sofia Forssten

Contact details
Sokeritehtaantie 20
Kantvik
Finland
02460

-
sofia.forssten@iff.com

Type(s)
Principal investigator

Contact name
Mr Mahadev Ramjee

Contact details
Panthera Biopartners Preston, 228 Garstang Road
Preston
United Kingdom
PR2 9RB
+44 (0)1772237822
mahadev.ramjee@panthera-bio.com

Additional identifiers

Integrated Research Application System (IRAS)
328119

Protocol serial number
CT001712

Study information

Scientific Title
Next generation probiotics for metabolic health: a double-blind, randomized, placebo-controlled safety trial, TS_NGP_SafetyA

Acronym
TS_NGP_SafetyA

Study objectives
A new Akkermansia strain has not yet been clinically tested, and thus this trial is required to verify its safety and tolerability. This study aims to obtain data on the safety and tolerability of orally consumed new Akkermansia strain over a 28-day intervention in a healthy population devoid of medical diagnoses or disorders.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 23/07/2024, West of Scotland REC 3 (Ground Floor, Ward 11, Dykebar Hospital, Grahamston Road, Paisley, PA2 7DE, United Kingdom; +44 (0)141 314 0212; WoSREC3@ggc.scot.nhs.uk), ref: 24/WS/0081

Primary study design
Interventional

Study design
Phase 0/1 prospective four-arm (parallel-group) double-blind randomized placebo-controlled multi-centre clinical trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Safety and efficacy of a potential new probiotic in healthy volunteers

Interventions
This is a phase 0/1 clinical trial, investigating the safety of a 4-week oral supplementation of a new Akkermansia strain in three different doses 1 x 10^9, 1 x 10^10 and 2 x 10^10 colony forming units (CFU)/day (1 capsule to be taken once per day in a fasting state), followed by a 4-week wash-out stage in a prospective, four -arm (parallel groups), double-blind, randomized, placebo-controlled, multi-centre clinical trial.

The centralized randomization list will be provided by EstiMates, according to their SOP 5. The randomization list will be created by an unblinded statistician, i.e., a Randomization Specialist, who will have no other role in the trial conduct. The Trial Statistician remains blinded until the database is locked. Randomization will be carried out using unstratified randomly permuted blocks at a ratio of 1:1:1:1. The randomization list will be provided to the Sponsor's manufacturer (Danisco USA Inc., Madison, WI, US) for IP labeling. IP will be sent to the trial sites fully blinded. No other personnel associated with the trial will have access to the randomization list until database lock.

Intervention Type
Supplement

Primary outcome(s)
Safety is measured by monitoring adverse events daily, gastrointestinal symptoms via the Gastrointestinal Symptom Rating Scale (GSRS) once per week, and stool frequency and consistency using a bowel frequency questionnaire and the Bristol Stool Scale Assessment daily.

Key secondary outcome(s)
1. Changes in safety biomarkers are measured using the following laboratory analyses at days 0, 14, 28 and 56:
1.1. Blood safety analyses: hemoglobin, hematocrit, red blood cells, white blood cells, platelets, urea, creatinine, bilirubin, minerals: calcium, phosphate, potassium, sodium, chloride, magnesium, and bicarbonate.
1.2. Urine safety analyses: aspect and color as per local lab, density, bilirubin levels, protein (albumin), glucose, ketones, nitrites, pH, and presence of red and white cells.
1.3. Liver function: alanine transaminase (ALT), gamma-glutamyltranspetidase (GGT), alkaline phosphatase (AP), aspartate aminotransferase (AST),
1.4. Tissue damage-related markers: Lactase dehydrogenase (s-LD), creatine kinase (p-CK)
1.5. High-sensitivity C-reactive protein (hs-CRP)

Completion date
01/10/2025

Eligibility

Key inclusion criteria
1. Provision of signed and dated informed consent form
2. Stated willingness to comply with all trial procedures and availability for the duration of the trial
3. Free-living females and males of age 25 to 65 years (limits included)
4. Low risk of metabolic syndrome based on the following parameters:
4.1. HbA1C 4.0 -– 5.6 % (20-42 mmol/ml)
4.2. LDL < 3.0mmol/l (< 116 mg/dl)
4.3. Total cholesterol < 5.0 mmol/l (< 193.4 mg/dl)
4.4. HDL > 1.0 in males and > 1.2 in females mmol/l (> 38.7 in males and > 46.4-mg/dl in females)
4.5. BMI 18.5 – 24.9 kg/m2
4.6. Waist circumference: males < 94 cm, females < 80 cm
4.7. Waist-hip-ratio: males < 0.95, females < 0.8
5. An individual who agrees to maintain their usual lifestyle throughout the trial, i.e., agrees not to change their dietary habits and level of exercise etc. during the trial
6. Females of child-bearing potential must agree to use medically approved methods for birth control including condoms with or without spermicides, hormonal contraceptives (estrogen and /or progestin products; either oral, intrauterine, or epidermal) or intrauterine device with copper. The contraceptive method should have been in place for at least 3 cycles before the beginning of the trial and should not be modified during the trial
7. Postmenopausal women aged 45 years and above who have not had a period for at least 12 months and are not using hormonal contraception. If on hormone replacement therapy, they must have been applying the estrogenic or estrogenic/progestin treatment for at least 3 months before the beginning of the trial.
8. Ability of the participant, in the investigator’s opinion, to comprehend the full nature and purpose of the trial including possible risks and side effects

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
25 Years

Upper age limit
65 Years

Sex
All

Total final enrolment
59

Key exclusion criteria

1. Having hypersensitivity or history of allergy to the trial product components, or a history of adverse effects, intolerance, or allergic reactions attributed to any medications
2. Suffering from a chronic disease (e.g., autoimmune disease, cancer, renal failure, HIV, immunodeficiency, hepatic or biliary disorders, arthritis, uncontrolled cardiac disease, terminal illness) or from an illness that may preclude the participant's ability to complete the trial or that may confound the trial outcomes according to the assessment by the investigator
3. History of heart failure with reduced left ventricular ejection fraction (LVEF) defined as any past measurement of LVEF ≤ 40%
4. Unstable heart failure with preserved ejection fraction, defined as: a) New York Heart Association (NYHA) class III-IV or, b) Hospitalisation or emergency room visit for heart failure during the past one year or, c) Need for intravenous diuretics in the outpatient setting within 6 months of Screening or, d) Concomitant treatment with a high dose of diuretics (i.e., furosemide 80 mg/day or equivalent)
5. Abnormal laboratory values at screening, including any of the following:
5.1. AST or ALT ≥ 5 × ULN (upper limit of normal)
5.2. Alkaline phosphatase > 2 × ULN
5.3. Impaired renal function defined as eGFR ≤ 60 mL/minute/1.73 m2 at screening (estimated according to the CKD Epidemiology collaboration) (Inker et al 2021)
5.4. Albumin < 3.5 g/dL (35 g/L)
5.5. INR ≥ 1.3 L
5.6. Any other clinically significant abnormalities in serum chemistry, hematology, or urinalysis results as judged by the investigator
6. Uncontrolled hypertension at screening and randomization, defined as mean systolic blood pressure >160 mm Hg or mean diastolic blood pressure >100 mm Hg (based on the average of 3 blood pressure readings if the first reading is outside of these limits).
7. History of diagnosed gastrointestinal complications at screening or randomization. (e.g., Crohn's disease, ulcer, IBS-mixed, IBS-constipation, IBS-diarrhea, celiac disease)
8. Prior abdominal surgery (e.g., gastric bypass, gastrectomy, gastric band, visceral surgery) at screening or randomization that, in the opinion of the investigator, may present a risk for the participant or confound trial results.
9. Clinically significant diagnosis of any eating disorder at screening or randomisation (e.g., anorexia, bulimia)that may impact the safety of the subject or the trial data as per investigator judgement.
10. Antibiotic course within 3 months before screening or any active infection during the screening period or ongoing chronic infection for the duration of the study.
11. Having a lifestyle deemed incompatible with the trial according to the investigator, e.g., a specific extreme diet (e.g., hypocaloric, ketogenic), intense physical activity > 10 hours/week.
12. Any self-declared clinically significant alcohol misuse (more than 14 units of alcohol per week)at screening or randomisationthat may impact the safety of the subject or the trial data.
13. Self-declared use of illicit drugs at screening or randomisationthat may impact the safety of the subject or the trial data as per investigator judgement.
14. Pregnant or lactating female, or pregnancy planned during the trial
15. The investigator believes that the individual may be uncooperative and/or noncompliant and should therefore not participate in the trial
16. Presenting a psychological or linguistic incapacity to understand and sign the informed consent
17. Participating in another clinical trial or in an exclusion period

Date of first enrolment

27/02/2025

Date of final enrolment
07/08/2025

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Panthera Biopartners- Preston
228 Garstang Road, Fulwood
Preson
England
PR2 9QB

Study participating centre
Panthera Biopartners- Rochdale
610 Bury Road
Rochdale
England
OL11 4AU

Sponsor information

Organisation
Danisco Sweeteners Oy

Funder(s)

Funder type
Industry

Funder Name
Danisco Sweeteners Oy

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 as, per the Informed Consent, participants in the study have not authorized the disclosure of their personal data outside the Investigator Site File and Trial Master File. It is stated in the ICF that “the results of the study may be submitted for presentation at one or more national or international scientific meetings and may be submitted for publication in a scientific journal. Upon request, participants can receive a summary sheet of study results after the study has been finalized.”. The data will be presented in summary tables (i.e., not possible to identify per participant) in the results publication

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results			14/09/2026	No	No
HRA research summary			30/10/2026	No	No