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Recovery study of L. casei DG® (Enterolactis® bevibile) in healthy children

Submission date
13/06/2018

Recruitment status
No longer recruiting

Registration date
28/06/2018

Overall study status
Completed

Last Edited
02/05/2019

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Lactobacillus paracasei, a normal component of healthy people's intestinal microbes, is a type of bacteria commonly used in dairy product fermentation and probiotics (health products containing bacteria). Other types of Lactobacillus are found in the intestines of animals, which means it is likely that they are important in how the bowel works. Intestinal microbes are involved in metabolism (energy production), nutrition, and protective immune responses. A previous study in adult healthy volunteers demonstrated the presence of the live L. casei DG® in faeces (solid waste from the bowel) up to 7 days after the volunteers stopped taking the product. The aim of the present study was to investigate the ability of L. casei DG® in a product designed for children to survive and grow in the intestines of children.

Who can participate?
Healthy children aged 3-12 years

What does the study involve?
All enrolled children received the same treatment. The drank one bottle of the Enterolactis® product each day for 7 days. Samples of their faeces were collected in special sterile containers during the week before they started taking the product, during the week they were taking the product and during the 2 weeks after they had stopped taking the product.
A diary was provided to the children or their parents or legal guardians at the screening visit. The diary was checked at each visit and was returned to the clinical staff at the final visit. During the whole study the subjects (or their parent(s)/legal representative(s) depending on the age and ability of the child), filled in a daily diary.

What are the possible benefits and risks of participating?
L. casei DG® (Lactobacillus paracasei CNCM I-1572; Enterolactis® as a drinkable product) is safe and well tolerated. In addition, no invasive procedures were performed during the study.
No specific benefits for the study participants were foreseen, except for the physical examination as part of the study procedures and a possible, although not certain, positive wellbeing effect.

Where is the study run from?
CROSS Research S.A. (Switzerland)

When is the study starting and how long is it expected to run for?
August 2017 to October 2017

Who is funding the study?
SOFAR S.p.A. (Italy)

Who is the main contact?
Dr. Walter Fiore, Medical Expert
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
CRO-PK-17-322; PSC-DS RECENT-BS 16

Study information

Scientific Title
Recovery study of L. casei DG® (Enterolactis® bevibile) in healthy children

Acronym
L. casei DG® - children

Study objectives

The primary objective of the study was to evaluate L. casei DG® (Lactobacillus paracasei CNCM I-1572; Enterolactis® in a drinkable formulationLactobacillus paracsei Enterolactis® bevibile) ability to transit alive through the gastrointestinal tract during product intake and to survive also after the end of product intake

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Cantonal Ethics Commitee Ticino, 24/07/2017, Project ID 2017-01231/CE 3246
2. Non-substantial amendment Nr.1, 17/08/2017

Study design
Single-centre open-label one-arm pilot study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Home

Study type(s)
Other

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Health condition(s) or problem(s) studied
Survival of Lactobacillus casei DG in the gut of children

Interventions
The study protocol specified a screening visit, a 1-week run-in phase and a 1-week treatment phase followed by a 2-week follow-up phase and a final visit.
All enrolled children received the same treatment, i.e. 1 bottle of Enterolactis® containing 1 billion live cells of L. casei DG®. The subjects drank one bottle of the investigational product daily for 1 week, i.e. for a total of seven doses (seven bottles). Upon opening, the content of the bottle's cap was directly mixed with the solution in the bottle to reconstitute the product. The solution was shaken well. The children drank directly the contents of the bottle, preferably under fasting conditions for at least 2 h, in the morning at least 10 min before breakfast. If the subject forgot or could not take the product in the morning, the bottle contents was consumed in the evening before going to bed and in any case at least 2 h after the last meal of the day. The subject should take the product always at the same time, i.e. either in the morning or in the evening, whichever time was more convenient.
Faecal samples were collected in special sterile containers, provided by the clinical staff to the children/parent(s)/legal representative(s), and were stored at home at approximately 2-8°C. The samples were collected at the following days or up to 2 days after each specified day: baseline,

Day 1, Day 4, Day 8, Day 11, Day 14, Day 17, Day 20. Then they were picked up by the courier as soon as possible after defecation. The samples were delivered to Dipartimento per gli Alimenti, la Nutrizione e l'Ambiente (DEFENS), Italy, taking into consideration that processing for primary variable analysis had to be completed by the laboratory within 24 h from sample production.
A diary was provided to the subjects/parent(s)/legal representative(s) at screening, was checked at each visit and was returned to the clinical staff at final visit/ETV. During the whole study the subjects (or their parent(s)/legal representative(s) depending on the age and ability of the child), filled in a daily diary where they confirmed:
1. Exclusion of forbidden foodstuffs
2. Occurrence of any AEs
3. Intake of any concomitant medications
4. Time of intake of the investigational product on Days 1-7
5. Day/time of defecation (all occurrences)
They also reported the following evaluations:
6. Digestive function
7. Faecal consistency on the Bristol stool scale
8. Response to the question on the product intake (Day 8).

Intervention Type
Supplement

Primary outcome measure
Faecal recovery of viable L. casei DG®, determined on the basis of L. casei DG® colony-forming units (CFU) count

Secondary outcome measures
1. Defecation frequency at baseline, during and after treatment (diary)
2. Faecal consistency at baseline, during and after treatment (using the Bristol stool scale)
3. Digestive function evaluation (diary)
4. Product intake global evaluation (question on Day 8 - diary)
5. Faecal microbiota (microbial composition) characterisation (by culture of faecal samples)

Overall study start date
03/10/2016

Completion date
04/10/2017

Eligibility

Key inclusion criteria
1. Aged 3-12 years inclusive
2. Not classified as overweight based on the applicable body mass index chart for sex and age (SSP SGP. Growing curves. http://www.swiss- paediatrics.org/sites/default/files/recommandations/courbes_de_croissances/pdf/perzentilen_2012_09_15_sgp_i.pdf. Accessed 20/06/2017)
3. Informed consent: informed consent of the parent(s)/legal representative(s) in accordance with Swiss regulations. Children aged ≥11 years provided informed consent; children aged from 3 to <11 years were not required to provide consent and were informed verbally
4. Full comprehension: ability of the children and/or their parent(s)/legal representative(s) to understand the full nature and purpose of the study, including possible risks and side effects;

ability of the children and/or their parent(s)/legal representative(s) to co-operate with the investigator and to comply with the requirements of the entire study

Participant type(s)
Healthy volunteer

Age group
Child

Lower age limit
3 Years

Upper age limit
12 Years

Sex
Both

Target number of participants
20

Total final enrolment
20

Key exclusion criteria
1. Clinically significant abnormal physical findings which could interfere with the objectives of the study
2. Unusual defecation frequency: on average more than 3 stools per day or less than 3 stools per week, as reported by the child/parent(s)/legal representative(s)
3. Food allergies (known or suspected); ascertained or presumptive hypersensitivity to the active principle and/or formulations' ingredients; history of anaphylaxis to drugs/food supplements or allergic reactions in general, which the investigator considered could affect the outcome of the study
4. Intake of antibiotics within 1 month of screening
5. Medications, including over-the-counter medications and herbal remedies within 2 weeks of the start of the study.
6. Significant history of renal, hepatic, gastrointestinal, cardiovascular, respiratory, skin, haematological, endocrine or neurological diseases that could interfere with the aim of the study. In particular:
6.1. Inflammatory intestinal chronic diseases
6.2. Intestinal diseases of infective origin
6.3. Viral or bacterial enteritis episodes in the 2 months before screening
6.4. Gastric or duodenal ulcer episodes in the 5 years before screening
6.5. Ongoing systemic infections
6.6. History of congenital infections
6.7. Neurological diseases
6.8. Metabolic diseases
6.9. Genetic diseases or chromosome anomalies
6.10. Primary or secondary immunodeficiencies
7. Participation in the evaluation of any investigational product in the 3 months before this study. The 3-month interval was calculated as the time between the first calendar day of the

month that followed the last visit of the previous study and the first day of the present study
8. Recent history of drug or alcohol abuse
9. Unusual diets or substantial changes in eating habits in the 4 weeks before this study or vegetarian
10. Consumption of probiotics/prebiotics during run-in, including fermented milk probiotics (traditional yoghurt was allowed), probiotics food supplements or any other probiotic-containing product or prebiotic food supplement starting on Day -9
11. Pregnant (females only): urine pregnancy test for children of child-bearing potential
12. Compliance: presence of conditions that in the Investigator's opinion could lead to non-compliance to study requirements

Date of first enrolment
29/08/2017

Date of final enrolment
30/08/2017

Locations

Countries of recruitment
Switzerland

Study participating centre
CROSS Research S.A. Phase I Unit
Via F.A. Giorgioli 14
Arzo
Switzerland
6864

Sponsor information

Organisation
SOFAR S.p.A.

Sponsor details
Via Firenze 40
Trezzano Rosa (MI)
Italy
20060

Sponsor type
Industry

Website
http://www.sofarfarm.it/

ROR
https://ror.org/04f3x2j17

Funder(s)

Funder type
Not defined

Funder Name
SOFAR S.p.A.

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
31/12/2018

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/12/2019	02/05/2019	Yes	No