Study Identification

Protocol ID: IRESP.PROB-2

Brief Title

"Clinical trial to evaluate the efficacy of *Lacticaseibacillus rhamnosus* CRL1505 in the prevention of upper respiratory tract infections in children".

Official Title

"Randomized, double-blind, placebo-controlled clinical trial to evaluate the efficacy and safety of *Lacticaseibacillus rhamnosus* CRL1505 in the prevention of upper respiratory tract infections in a healthy pediatric population".

Study Status

Study Start

First patient included: 17/12/2024.

Study Completion:

End of the follow-up period of the last included patient: The study is expected to be completed in March 2027

Results and completion: July 2027

Sponsor/Collaborators

Sponsor: Centro Sperimentale del Latte S.r.l

Collaborators: MiBioPath Research Group – UCAM

Ethics Committee

Board Affiliation: Ethics Committee of the Catholic University San Antonio de Murcia (UCAM).

Approval number: 26/07/24 – CE072408

Study Description

Brief Summary

Randomized, double-blind, placebo-controlled, parallel-group, clinical trial to assess the efficacy of the intake of a probiotic product composed of *Lacticaseibacillus rhamnosus* CRL1505 strain in reducing or preventing upper respiratory tract infections (URTIs) in a healthy pediatric population.

Keywords: prevention, upper respiratory tract infections, probiotics, microbiota, microbiome

Description

Randomized, double-blind, placebo-controlled, parallel-group, clinical trial.

The study aims to demonstrate the efficacy of the intake of a probiotic product composed of *Lacticaseibacillus rhamnosus* CRL1505 strain in reducing or preventing upper respiratory tract infections in a healthy pediatric population.

The clinical trial has an intervention period of 12 weeks and a post-treatment follow-up period of 4 additional weeks (16 weeks in total).

The study aims to demonstrate the efficacy and safety of consuming the probiotic strain *Lacticaseibacillus rhamnosus* CRL1505 in the prevention and reduction of the severity and duration of URTI (upper respiratory tract infections) episodes in a healthy pediatric population.

A total of 268 participants aged 3 to 12 years will be recruited and randomized into two treatment groups in a 1:1 ratio (134 participants in the PROBIOTIC GROUP and 134 participants in the PLACEBO GROUP). The two intervention groups will differ based on the treatment received: probiotic or placebo, both of which will have a similar appearance.

The study will focus on a healthy pediatric population; therefore, the exclusion criteria will eliminate children with significant acute or chronic diseases and those with an immunocompromised condition. Additionally, children receiving continuous pharmacological treatment or those who have consumed dietary supplements that could influence the study results within the four weeks prior to inclusion will be excluded. However, if these children can discontinue such treatments, they may participate in the clinical trial after a washout period. Continuous regular medication that is deemed not to influence the study outcomes regarding the efficacy of the investigational product will be allowed.

Participants will be required not to modify their diet or physical activity during the course of the study.

The inclusion process will take place during winter months, to ensure that the study coincides with the months of highest URTI incidence.

Since this clinical trial will be conducted in minors, continuous evaluation will be the responsibility of the parents. They will be instructed to complete an online questionnaire daily, which will allow data collection to assess the efficacy and safety variables.

Study Design

Study type: Interventional

Interventional Study Model: Randomized, double-blind, placebo-controlled with parallel assignment

Number of arms: 2

Masking: Double (Participant and Investigator)

Allocation: Randomized

Enrollment: 268 patients

Arms and Interventions

Experimental arm

Probiotic group: The probiotic product is provided in 2g sticks containing the strain *Lacticaseibacillus rhamnosus* CRL1505 at a concentration of ≥ 1.0E+8 CFU/g, with corn starch and maltodextrin as excipients. The test product is classified as a food supplement and not as an investigational medicinal product

Placebo comparator

Placebo group: The placebo product is provided in 2g sticks of corn starch and maltodextrin

Outcome measures

Primary Outcome Measure

- Number of URTIs, with the following endpoints:
  - Difference in the proportion of patients who were diagnosed with at least 1, 2 and 3 URTI during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.
  - Difference in the average number of URTI episodes per participant during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups

A subgroup analysis of these primary endpoints will be conducted, distinguishing between the different types of URTIs detected, primarily the common cold and influenza. This sub-analysis will only be performed if a considerable number of URTIs other than the common cold are recorded

Secondary Outcome Measures

- Difference in the proportion of participants who experienced URTI complications (bacterial superinfections such as pneumonia, otitis media, and acute sinusitis) during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.
- Difference in the average number of days with a URTI episode per participant (days with URTI/participants) during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.
- Difference in the average number of days until the onset of the first URTI episode during the intervention period (12 weeks) between the study groups.
- Difference in the average duration of each URTI episode (mean ratio of days with URTI/URTI episodes for each participant) during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the URTI-free time rate (proportion of accumulated days in which participants do not experience URTI relative to the total number of days) during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the average score of each symptom evaluated on the Jackson scale (sore throat, nasal congestion, runny nose, cough, sneezing, headache, muscle pain, chills) per day of common cold episode during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the average number of days with fever per participant during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the proportion of participants who received antibiotic treatment during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the average number of days with antibiotic treatment per participant during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the proportion of URTI episodes in which participants received symptomatic medication (to relieve URTI symptoms) during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the proportion of URTI days in which participants received symptomatic medication (to relieve URTI symptoms) during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the proportion of participants who experienced gastrointestinal infections during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the school absence rate (proportion of accumulated school absence days due to URTI relative to the total number of days) during the intervention period (12 weeks) and the total follow-up period (16 weeks) between the study groups.

- Difference in the change in the "average salivary IgA concentration" after 12 weeks of intervention compared to baseline between the study groups.

Safety Variables

- Incidence and severity of all Adverse Events.
- Incidence of Severe Adverse Events.
- Incidence and severity of Adverse Events related to the study product.

- Incidence and severity of Adverse Events leading to study withdrawal.
- Rate of withdrawal due to intolerance to study product.

Eligibility

Inclusion Criteria

- Healthy children aged 3 to 12 years.
- Signed Informed Consent by the parents

Exclusion Criteria

- Chronic pathological conditions, such as chronic respiratory diseases (asthma, chronic bronchitis, etc.), chronic heart diseases, chronic neurological diseases (psychomotor impairment, etc.), chronic liver diseases, chronic kidney diseases, chronic gastrointestinal diseases, hematological disorders, etc., or any other disease or condition that the investigator considers to significantly affect the health of the participating child.
- Metabolic disorders, such as diabetes mellitus, obesity, etc.
- Immunodeficiency, including HIV infection, chronic corticosteroid treatment, etc.
- Nasal polyps, nasal ulcers, or other conditions that may cause nasal obstruction.
- Regular use of medications or dietary supplements that may influence the study outcomes (immunosuppressants/immunostimulants, including echinacea supplements, analgesics, anti-inflammatory drugs, antitussives/expectorants, flu preparations, decongestants, antibiotics, antihistamines, probiotics, etc.) within the 4 weeks prior to the start of the clinical trial.

Locations

Catholic University of Murcia (UCAM). MiBioPath Research Group

Murcia, Spain

Contact: Vicente Navarro López

E-mail: vicente.navarro@bioithas.com

Contact: Pedro Sánchez Pellicer

E-mail: pedro.sanchez@bioithas.com

Contacts

Central Contact Person

Juan Gabriel Agüera Santos

Telephone: +34623022586

E-mail: juan.aguera@bioithas.com