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A double-blind, randomized, parallel, placebo-controlled study to evaluate the efficacy and safety of a probiotic containing Lactobacillus paracasei (eN-Lac®) for the treatment of children with perennial allergic rhinitis (year-round nose irritation caused by allergy)

Submission date
27/10/2022

Recruitment status
No longer recruiting

Registration date
28/10/2022

Overall study status
Completed

Last Edited
09/11/2023

Condition category
Ear, Nose and Throat

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

Plain English summary of protocol

Background and study aim
Allergic rhinitis is known as one of the most prevalent atopic diseases worldwide ranging from 5 to 22% incidence in different countries. This disease is and immune reaction to allergens, typically found to be house dust mites, animals, and pollen. Clinical signs and symptoms of allergic rhinitis include rhinorrhea, nasal congestion, sneezing, and nasal and ocular itching. Except for avoiding allergen contact and desensitization approach, management of allergic rhinitis is focusing on symptoms control. Approaches to allergic rhinitis control are mainly by the use of anti-histaminic agents. However, continuing use of anti-histamines may post safety concerns, especially their long-term use in younger patients under the age of 18 years old. Probiotics as an immune-modular via balance Th1 and Th2immune activities, namely, prompting Th1 effects and inhibiting Th2 activity, may produce control and alleviation of allergic rhinitis symptoms. It is therefore a potentially more desirable manner considering the safety nature of probiotics being GRAS (Generally recognized as safe) and endogenous.
This study is an phase II study aiming to establish a dose-response relationship for Lactobacillus Paracasei in the treatment of perennial allergy rhinitis of children. Three dose levels are incorporated into the design for establishing a dose-response curve. The treatment duration is 12 weeks but an extension for another 9 months follow-up in to reveal the longer treatment efficacy and safety profiles will be employed. The outcome derived from this study will be used to design the future phase III study to confirm the efficacy and safety profiles of Lactobacillus Paracasei for perennial allergy rhinitis treatment.

Who can participate?
Children with age 5-16 years old who suffer from perennial allergy rhinitis

What does the study involve?
In the screening stage (Visit 1; -10 to -4 days of first treatment day), participants will be asked to join this study while they are at a clinic, and all of the parents or legal representatives of participants will need to agree with them to take part in this study since the participants are all underage. In Randomization visit (Visit 2; week 0). All eligible subjects are allocated to one of four groups. In the evaluation visits, those in the first group need to intake one capsule of Lactobacillus paracasei eN-Lac® 2*108 CFU/cap once a day. Those in the second group need to intake one capsule of Lactobacillus paracasei eN-Lac® 2*109 CFU/cap once a day. Those in the third group need to intake one capsule of Lactobacillus paracasei eN-Lac® 1010 CFU/cap once a day. And those in the fourth group need to intake one matching placebo capsule once daily. During the evaluation visit, they will encounter 3 visits including Visit 3 (14±3 days), Visit 4 (28±7days), Visit 5 (56±7days), and Visit 6 (84±7days) will be the final visit. . After 12 weeks of consumption of capsules, all groups will finish their evaluation visit and change into safety follow-up visits (Visit 7; 24±4 weeks, Visit 8; 48±4 weeks) to record any adverse event occurred after the trial. The follow-up visit can be conducted by telephone contact.
Body weight, vital signs, physical examination, blood, and urine sample collection and lab test, allergy test, NTSS, and history medication record will be performed during the study. DRC (Daily Record Card) will be given to participants to record any side effects and any medication will be in the trial.

What are the possible benefits and risks of participating?
According to our clinical research results, the participants who are randomized to the eN-Lac® groups may enhance their immune response to pathogens and reduce the hypersensitivity reaction to allergens further improving their symptoms of perennial allergy rhinitis. Since the alteration in the flora of the gastrointestinal tract, diarrhea, constipation, and abdomen bloating might occur, these symptoms usually can be relieved in a week.

Where is the study run from?
The interval study is sponsored by GenMont Biotech Incorporation and conducted by Virginia Contract Research Organization Co., Ltd entrusted by GenMont, and takes place in MacKay Memorial Hospital and Chang Gung Children’s hospital (Taiwan)

When is the study starting and how long is it expected to run for?
October 2006 to July 2007

Who is funding the study?
GenMont Biotech Incorporation (Taiwan)

Who is the main contact?
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Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
GMENA040813

Study information

Scientific Title
Lacticaseibacillus paracasei eN-Lac® ameliorates allergic airway inflammation in children with allergic rhinitis: a double-blind, randomized, placebo-controlled trial

Study objectives
Lactobacillus species, namely, Lactobacillus casei and Lactobacillus paracasei, have shown to be particularly beneficial due to the known properties of gut wall adhesion and the ability to produce bacteriocin, hydrogen peroxide, and biosurfactants. The ability of Lactobacillus casei to decrease mucosal permeability in the small intestine and diminish the production of harmful

materials in the large intestine may explain partially the beneficial effect on the host's body. The preclinical study had shown decreased In the previous randomized, double-blind, placebo-controlled trial, after 30-days treatment patient treated with fermented milk containing Lactobacillus paracasei LP-33 (original name of eN-Lac®) can improve the quality of life of patients with perennial allergy rhinitis, the severity of rhinitis at the baseline visit was comparable between the LP-33 and placebo group, the LP-33 group had significantly higher scores for frequency if and bother caused by nose symptoms (p=0.044 and p=0.036, respectively). IgE measures also provided encouraging results that the LP group showed a statistically significant decrease from baseline after the 12-week treatment period (p=0.032). We conducted this pilot trial using gut microfloral ecosystem and showed that this strain had a positive impact on the quality of life of perennial rhinitis sufferers. With positive benefits from consumption of the probiotic LP-33 to allergic patients and without any severe adverse effects emerging, Indicate probiotic treatment probably can be another choice that may prove efficient and cause rare pleasant side effects.
This clinical trial will be conducted to evaluate three dose levels incorporated into the design for establishing a dose-response curve, including the dose-response relationship, determine the optimal dose, and evaluate the efficacy, safety, and tolerability profiles of eN-Lac®. The proper dose level is expected to be determined from this study result.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 13/11/2006, Joint Institutional Review Board (JIRB, c/o Taipei Veterans General Hospital, VAC No. 201, Sec 2, Shih-pai Road, Taipei City, Taiwan 11217 ROC; +886-2-28737133; jirb@jirb.org.tw) ref: 05-016-A

Study design
Two center interventional randomized double-blind placebo-controlled study Phase II

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Perennial allergic rhinitis (PAR)

Interventions
Subjects who meet all eligible requirements for entry into the study will be randomized into one of the four treatment groups in 1:1:1:1 ratio as shown below:

1. One capsule of Lactobacillus paracasei (eN-Lac®) 2 x 10(8) CFU per capsule, once daily
2. One capsule of Lactobacillus paracasei (eN-Lac®) 2 x 10(9) CFU per capsule, once daily
3. One capsule of Lactobacillus paracasei (eN-Lac®) 1 x 10(10) CFU per capsule, once daily
4. One matching placebo capsules, once daily
The treatment period is 12 weeks.

Intervention Type
Supplement

Primary outcome measure
Dose response of LPmeasured using net change in mean NTSS (Nasal Total Symptom Score) at the 12th week treatment visit (compared to baseline). NTSS is recorded daily by the patients using a DRC (Daily Record Card).

Secondary outcome measures
1. Net change of the 2nd, 4th, and 8th week evaluations compared to the baseline on NTSS
2. Net change of the 2nd, 4th, 8th and 12th week evaluations compared to the baseline on each individual symptom score rated in the NTSS items
3. Net change of the 2nd, 4th, 8th and 12th week evaluations compared to the baseline on NTSS by investigator's evaluation at site
4. Net change of the 2nd, 4th, 8th and 12th week evaluations compared to the baseline on each individual symptom score rated by NTSS by investigator's evaluation at site
5. Global assessment by the investigator as categorized into 4 levels of complete relief, partial relief, no relief, worse.
6. Net change of the serum interferon-γ (IFN-γ) concentration during the treatment period (IFN-γ at Visit 6 – IFNγat baseline)
7. Net change of the serum total IgE (Immunoglobulin E) concentration during the treatment period (IgE at baseline-IgE at Visit6)

Safety endpoints:
1. Vital signs change: The vital signs including blood pressure, pulse rate, respiratory rate and body temperature will be assessed for changes compared to baseline
2. Adverse event incidence: Adverse event will be recorded for each of the visits starting from the baseline visit
3. Physical examination changes: physical examinations will be performed for the 4th and 12th week visit. Changes in physical examination results for these two during-treatment visit will be considered as one of the safety observations.
4. Blood laboratory test result changes: The blood laboratory tests including the following items will be tested periodically: WBC (White blood cell) with differential counts, RBC (Red Blood Cell), hemoglobin, hematocrit, platelet , MCV (Mean Corpuscular Column), MCH (Mean Corpuscular Hemoglobin), MCHC (Mean Corpuscular Hemoglobin Concentration), AST (Aspartate aminotransferase), ALT (Alanine aminotransferase), albumin, total protein, total bilirubin, Alkaline phosphatase, LDH (Lactate dehydrogenase), creatinine, BUN(Blood Urea Nitrogen), uric acid, glucose, Potassium, Calcium, Phosphorus, Sodium, Chloride, Magnesium, and Iron.
5. Urine laboratory test results changes (Qualitative changes): The urine laboratory tests including the following items will be tested at the 4th and 12th week visit: WBC, RBC, pH, protein, glucose, and ketone body.

Overall study start date
20/10/2006

Completion date
12/07/2007

Eligibility

Key inclusion criteria
1. Subjects with age of 5-16 years old (inclusive)
2. Subjects with a history of PAR for at least 1 year
3. Subjects with either one of the following test results (test results within 12 months before study are acceptable)
3.1. Positive skin-prick test reaction (wheal 3mm larger than the diluents control)
3.2. Positive reaction determined by the CAP or MAST(Multiple allergosorbent test) system
4. Subjects with mean NTSS of no less than 5 throughout the screening period (4 to 10 days); at least 4 days should be recorded during the screening period; and the NTSS of the day before day-0 (first dosing day) visit is no less than 5
5. Subjects' parents or their legally acceptable representatives have signed the written informed consent form

Participant type(s)
Patient

Age group
Child

Lower age limit
5 Years

Upper age limit
16 Years

Sex
Both

Target number of participants
Approximately 140 subject will be enrolled for the study treatment. The study aims to complete at least 120 analyzable for the 4 treatment arms, from a total of 2centers in Taiwan.

Total final enrolment
137

Key exclusion criteria
1. Subjects have clinically significant abnormalities laboratory results as determined by the investigator (Tests performed during 14 days prior to Visit 1 or during baseline period can be used for evaluating this criterion)
2. Subjects with acute or significant chronic sinusitis, severe persistant asthma, congenital immunodeficiency, neuropsychiatric disorders, immune-compromised massive wound in the oral cavity, use of rhinitis medications, and chronic use of tricyclic antidepressants
3. Subjects who need to take prohibited medications during the study or took the medications within 30 days prior to the screening visit:
- Parenteral or oral corticosteroids

- Nasal corticosteroids
- Topical use of flurandrenolide
- Topical use of clobetasol propionate
- Topical use of halobetasol propionate
- Astemizole
- Ketotifene
- Nedocromil or Sodium cromoglycate
- Loratadine
- Cetirizine
- Antileukotrienes
- Other H1 antihistamine
- Nasal decongestant
- Any food supplements including LP(Lactobacillus paracasei)

4. Subject is undergoing desensitization therapy within 3 months prior to the screening visit or with vasomotor rhinitis
5. Subject participated investigational drug trial within 4 weeks before entering this study
6. Patients are pregnant or lactating or plans to become pregnant
7. Subjects with any other serious disease considered by the investigator not in the condition to enter the trial

Date of first enrolment
20/10/2006

Date of final enrolment
12/07/2007

Locations

Countries of recruitment
Taiwan

Study participating centre
MacKay Memorial Hospital
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Study participating centre
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Funder(s)

Funder type
Government

Funder Name
Ministry of Science and Technology, Taiwan

Alternative Name(s)
Ministry of Science and Technology, R.O.C. (Taiwan), Ministry of Science and Technology of Taiwan, MOST

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Taiwan

Results and Publications

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

Intention to publish date
01/12/2022

Individual participant data (IPD) sharing plan
The datasets generated during and/or analyzed during the current study are not expected to be made available due to commercial confidentiality

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file		17/10/2006	28/10/2022	No	No
Results article		28/02/2023	09/11/2023	Yes	No