ISRCTN93895684 https://doi.org/10.1186/ISRCTN93895684

A selected probiotic formula to reduce flu-related symptoms in vaccinated elderly people

Submission date
05/11/2020

Recruitment status
No longer recruiting

Registration date
12/11/2020

Overall study status
Completed

Last Edited
24/08/2022

Condition category
Respiratory

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

Plain English summary of protocol

Background and study aims
It has been recognized for many years that people 65 years and older are at high risk of developing serious complications from flu compared with young, healthy adults. This risk is due in part to changes in immune defences with increasing age. While flu seasons vary in severity, during most seasons, people 65 years and older bear the greatest burden of severe flu disease. In recent years, for example, it has been estimated that between 70 percent and 85 percent of seasonal flu-related deaths have occurred in people 65 years and older, and between 50 percent and 70 percent of seasonal flu-related hospitalizations have occurred among people in this age group. Flu vaccination is the best way to protect against flu and its potentially serious complications, but such an approach does not exempt vaccinated subjects to contract flu, either because the flu season lasts for many months and flu viruses can change during the winter season and as far as old people are concerned, because to age-related changes in the immune systems.

Between the complementary approaches to preserve elderly people from experiencing the typical flu-related symptoms, or common infectious disease, even after vaccination, the use of probiotics could play an interesting role, as it has been reported that administration of probiotics stimulate the immune response through a complex network of biological interactions and therefore it is foreseen that administrating a mixture of specific strains of probiotics could achieve better results.

Who can participate?
Elderly people between 60 and 80 years old.

What does the study involve?
Participants are randomly assigned to two groups and will either receive a probiotic stick treatment or a stick of the same size without the active ingredients. Participants will not know which group they have been assigned to and therefore which treatment they are receiving. Both groups will take one stick every day for 28 days. Stool and salivary samples will be collected at the beginning of the study, after the 28 days of receiving treatment, and then again after a further 28 days. Throughout the whole study, all participants will also be asked to complete a questionnaire about the Common Infectious Diseases (CID) symptoms they are having.

What are the possible benefits and risks of participating?
Participants who take the probiotic mixtures could benefit from an improvement of CID symptoms and less constipation. There are no notable risks involved in taking part in this study.

Risks associated with the intake of the product are considered from low to very low, in absence of allergy or intolerances to the product ingredients. Other ingredients in the formula of the product are commonly used in dietary supplements. No measurements carried out are invasive, stool and saliva samples only will be collected.

Where is the study run from?
Complife Italia Srl (Italy)

When is the study starting and how long is it expected to run for?
From October 2018 to May 2019

Who is funding the study
Regione Lombardia (Italy)

Who is the main contact
Dr. Francesco Tursi
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
E HU 093-0090 19 003L_2018_NATURHA

Study information

Scientific Title
A multistrain probiotic formulation to enhance resistance to common infectious diseases in flu-vaccinated health free-living elderly subjects, modulating gut microbiota diversity

Acronym
WELLDERLY

Study objectives
The selected probiotic formulation will be clinically effective in reducing flu-related symptoms in vaccinated elderly people. Microbiota modulation and immune systems activation will be evaluated in order to shed light on the mechanism of action of the treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/01/2019, Independent Ethical Committee for Non-Pharmacological Clinical Study Trials (Via XX Settembre 30/4, 16121 Genova, Italy; +39(0)10 5454842; a. scudieri@studinonfarmacologici.it), ref: 2018/14

Study design
Double blind, multi-centre randomized, placebo-controlled parallel-group clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home

Study type(s)
Treatment

Participant information sheet
See additional file ISRCTN93895684_PIS_v1_17Jan2020 (added 02/12/2020)

Health condition(s) or problem(s) studied
Influenza, common infectious disease symptoms in flu-vaccinated elderly subjects

Interventions

50 elderly subjects, flu-vaccinated according to the national scheme, were enrolled and equally allocated (1:1) to either the placebo or probiotic group using a computer generated restricted randomized list.

Before the beginning of the study, fecal and saliva samples were collected from all subjects, a questionnaire for registering CID symptoms was distributed to subjects who were informed by the physician on how to fill it.

Subjects from the placebo group took a stick containing excipients. Subjects from the probiotic group took a stick containing the probiotic mixture (Lactobacillus plantarum, Bifidobacterium animalis subs. lactis, Bifidobacterium longum subs. infantis, Bifidobacterium longum subs. longum)

All participants took one stick a day, with a glass of water, away from meals, for 28 days. All participants were asked to return to the study centers 28 days after the last products intake for the follow-up evaluations

Intervention Type
Supplement

Primary outcome measure
1. Common Infectious Disease (CID) symptoms either as the number of subjects who have CID symptoms or as number of days with the presence of CID symptoms as recorded in a study diary at baseline and 28 days
2. Calprotectin levels measured using an ELISA assay on stool samples collected at baseline and 28 days
3. Beta-defensin 2 levels measured using an ELISA assay on stool samples collected at baseline and 28 days
4. IgA levels measured using an ELISA assay on salivary samples collected at baseline and 28 days
5. Total Antioxidant Capacity measured using a FRAP assay on salivary samples collected at baseline and 28 days
6. Gut microbiota composition determined using V3-V4 16S NGS sequencing on DNA from stool samples collected at baseline and 28 days

Secondary outcome measures
1. CID symptoms measured as the number of subjects and number of days with CID symptoms between baseline and 56 days
2. Calprotectin levels measured using an ELISA assay on stool samples collected at 56 days
3. Beta-defensin 2 levels measured using an ELISA assay on stool samples collected at 56 days
4. IgA levels measured using an ELISA assay on salivary samples collected at 56 days
5. Total Antioxidant Capacity measured using a FRAP assay on salivary samples collected at 56 days
6. Gut microbiota composition determined using V3-V4 16S NGS sequencing on DNA from stool samples collected at 56 days

Overall study start date
02/10/2018

Completion date
13/05/2019

Eligibility

Key inclusion criteria
1. Aged between 60 and 80 years on the day of inclusion
2. Able to comply with all the trial procedures
3. Inoculated with an influenza vaccine
4. Body Mass Index (BMI) between 18.5 and 24.99
5. Willing to not vary the normal daily routine (such as lifestyle and physical activity)
6. Willing to not alter their usual diet or fluid intake during the trial periods
7. Willing to follow the proposed alimentary supplement for all the study time
8. Willing to use during all the study period only the product to be tested
9. Willing to not use products likely to interfere with the product to be tested
10. Aware of the study procedures and signed an informed consent form

Participant type(s)
Healthy volunteer

Age group
Senior

Sex
Both

Target number of participants
50

Total final enrolment
75

Key exclusion criteria
1. Recently involved in any other similar study
2. Contraindications to influenza vaccinations
3. Undergoing treatment related to immune system modulation in the past 4 weeks
4. Therapy for immunosuppressants for >2 weeks, either currently or stopped <3 months before inclusion
5. Received an influenza vaccination <1 year before inclusion
6. Current antibiotic treatment
7. History of chronic medical condition such as congenital heart disease, liver or kidney disease, or immune deficiency
8. Probiotic treatment within the 6 months before enrollment
9. Severe concurrent diseases
10. Drug abuse and/or alcohol abuse
11. Use of fiber products within the last 6 weeks
12. Dietary intake exceptionally high in plant-based, high fiber foods (such as fruits, vegetables, beans, whole grains, and fortified foods), including those following a strict vegetarian diet
13. Dietary intake of probiotics
14. Pre-existing hypersensitivity to components contained in the probiotic
15. Any condition that the principal investigator deems inappropriate for participation
16. Adult protected by the law (under guardianship, or hospitalized in a public or private institution, for a reason other than the research, or incarcerated)

Date of first enrolment
20/02/2019

Date of final enrolment
18/03/2019

Locations

Countries of recruitment
Italy

Study participating centre
Complife Italia Srl
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Study participating centre
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Sponsor type
Industry

Website
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Funder(s)

Funder type
Government

Funder Name
Regione Lombardia

Results and Publications

Publication and dissemination plan
A paper will be published in relevant international peer-reviewed journals.

Intention to publish date
30/11/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored in a non-publically available repository.

The investigator will allow direct access to all relevant files (for all subjects) for the purpose of verifying entries made in the data collecting sheet, and assist with the monitor’s activities, if requested. The subject must have consent to their records being viewed by sponsor-authorized personnel, and by local and possibly foreign Competent Authorities. This information should be included in the informed consent documents. Data must be entered onto collecting data sheet. All forms must be completed in blue ballpoint pen. All study documents must provide adequate verification of the content of the collecting data sheet. Definition of source data and source documents are given below:

Source Data: All original records and certified copies of original records of clinical findings, observations, or other activities necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies)

Source Documents: Original documents, data and records (subject file, collecting data sheet notes, evaluation check list)

All information, data and results of the study are confidential. All people having access to such data are informed of its confidentiality. In all cases, nominative information shall not be transmitted to the study sponsor. Whenever a subject name is revealed on a document required by the Sponsor (e.g., photographs) the name must be blacked out permanently by the site personnel, leaving the initials visible, and annotated with the subject number as identification. Data capture is performed by Complife Italia under Microsoft® Excel 2010 (vers. 14.0.4760.1000; Microsoft, USA) worksheet running on Microsoft® Windows 8.1 Professional (Microsoft, USA). Data entry and quality control are performed by two different persons. Calculated cells and formulas in Excel are also checked by the quality assurance. Statistical analysis was carried out using NCSS 10 statistical software (NCSS, LLC. Kaysville, Utah, USA) running on Windows Server 2008 R2 Standard (Microsoft, USA).

Record Archiving and Retention:
An original copy of all the data of the study (signed protocol, safety assessment letter of the Sponsor, case study report form, extracted raw data, administrative file including all the correspondence) is kept in the records of the Complife Italia for 10 years. The archives are destructed only after reception of a written and signed permission from the Sponsor. However, these documents should be retained for a longer period if required by the applicable regulatory requirements or by an agreement with the Sponsor. The investigator should take measures to prevent accidental or premature destruction of these documents. The archiving arrangements will be addressed by the monitor when closing-out the site. The Sponsor will inform Complife srl, in writing, as to when these documents no longer need to be retained.

IPD sharing plan summary
Stored in repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v1	17/01/2020	02/12/2020	No	Yes
Results article		20/06/2022	24/08/2022	Yes	No