Evaluation of Longevity Diet and Fasting Mimicking Diet programs on body composition, disease risk factors, and aging markers: a randomized clinical trial

NCT number

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INFORMATION SHEET AND INFORMED CONSENT FORM FOR PATIENT PARTICIPATION

IN A CLINICAL TRIAL

Official title of the clinical trial Effects of the Fasting-mimicking Diet and the Longevity Diet on Body Composition, Risk Factors for Age-related Diseases and Aging Markers: a Randomized Clinical Trial.
Official title of the clinical trial in more understandable terms for the patient Analysis of the effects of a low-calorie diet and longevity diet to slow down human aging
Structure-context in which the experimentation will take place Participants will be recruited in three municipalities in the province of Reggio Calabria (Molochio, Varapodio, Oppido Mamertina, and possibly other municipalities within a radius of 20 km) with the support of nutrition specialists. After enrollment, each participant will follow the diet assigned at their home.
Coordinating center (if different from the structure in which the trial will take place) and coordinator of the clinical trial Coordinator center at the **Valter Longo Foundation** Experiment Coordinator Dr.ssa Romina Inès Cervigni (Valter Longo Foundation, European Longevity Institute, Milan), Prof. Valter Longo (IFOM- FIRC Institute of Molecular Oncology Foundation, Milan)
Protocol Registration in which the trial has been registered or will be registered (if applicable) and any identification code if available Identification code _____ Protocol registration_____
Principal Investigator (indicate the local Trial Manager) **Name: Prof. Alberto Montesanto** **Affiliation: University of Calabria**
Sponsor / Financing Body Province of Reggio Calabria
Ethical Committee University of Calabria

This document consists of the following sections:

A. INTRODUCTION

B. INFORMATION SECTION. SUMMARY OF THE TRIAL: KEY INFORMATION

C. INFORMATION SECTION. FURTHER INFORMATION

D. EXPRESSION OF CONSENT SECTION

ATTACHMENTS

ADDITIONAL DOCUMENTS

Dear Mr/Mrs/Ms, the information contained in the following information sheet is very detailed. We ask you to accept to participate in the trial ONLY after having carefully read this information sheet and having had a FULL INTERVIEW with a member of the experimentation group who will have to dedicate the NECESSARY TIME to fully understand what is proposed to you.

A. INTRODUCTION

Dear Madam / Sir,

We offer you to participate in the clinical trial, which we illustrate below.

It is your right to be informed about the purpose and characteristics of the trial so that you can make an informed and free decision whether to participate or not.

This document aims to inform you about the nature of the trial, the purpose it proposes, what participation will entail for you, including your rights and responsibilities.

Please read the following carefully. The researchers involved in this project that are indicated at the beginning of this document, are available to answer your questions. No question that comes to your mind is trivial: don't be afraid to ask!

You can discuss the proposal contained in this document with your family doctor, your family and other people you trust. Take your time to decide. You can take home an unsigned copy of this document to think about it or to discuss it with others before deciding.

If you decide not to participate in the trial, you will still receive the best possible care for patients with your condition / disease.

Refusal will in no way be interpreted as a lack of trust.

Once you have read this form and have received answers to any questions and decided to participate in the trial, you will be asked to sign a consent form, of which you will receive a hard copy of.

The Principal Investigator

B. INFORMATION SECTION.

OVERALL SUMMARY OF THE TRIAL: KEY INFORMATION (no more than 1-2 pages)

This section has the objective of briefly addressing the key aspects of the experimentation which it proposes to join. The following sections will provide more details to give you the possibility to express or not a fully informed consent to your participation in the trial.

- Why am I being asked to participate in this experimentation?

We are asking you to participate in a clinical trial funded by the Province of Reggio Calabria because you have some clinical characteristics that will be better specified in section

- What are the objectives of the experimentation? How many centers and patients will take part in it?

The experimentation is done to answer this question "is it possible to induce beneficial effects on body composition and slow down the aging process through two specific controlled nutritional interventions?": We are doing this experimentation to understand if two diets are balanced and already tested in other studies can reduce fat mass and reduce / slow down the effects of aging. It is a low-calorie diet and a diet of longevity. The trial will take place in three municipalities in the province of Reggio Calabria (Molochio, Varapodio, Oppido Mamertina) with the support of nutrition specialists under the responsibility of Dr. Romina Inès Cervigni (Valter Longo Foundation, Milan), Prof. Valter Longo (IFOM- FIRC Institute of Molecular Oncology Foundation, Milan) and Dr. Alberto Montesanto (University of Calabria). 501 volunteers will be recruited with the aim of verifying whether the nutritional interventions mentioned above are able to modify the body composition and to reduce the percentage of fat mass; in the event that the number of participants enrolled in the study is inadequate, the recruitment activities will also be extended to neighboring municipalities in 20km from Varapodio.

In addition to the measurement of fat, through the analysis of the blood sample that you will provide us, we will be able to understand if the diet to which you will be subjected is able to (ii) reduce cholesterol levels, level, IGF-1, inflammation markers, (iii) inducing protective changes on biological aging (iv) reduce the use of hypoglycaemic or antihypertensive drugs and (v) improve the quality of sleep. Through the analysis of the DNA that will be isolated from the blood that you will provide us during the visits provided for by the study, the length of telomeres in leukocytes will be measured with appropriate advanced investigations, a predictive biomarker of aging and many age-related diseases. The analysis of the blood sample will be carried out at the Clinical Institute "Prof. Dr. R. De Blasi" srl located in Via Torrione Prol.to n. 55, 89123 Reggio Calabria, while the genetic investigations at the Genetics laboratory of the University of Calabria.

- Is it my free choice to decide whether to participate or not?

You can freely choose whether to participate in the experimentation or not. Even after accepting, you can change your mind at any time

- What happens if I decide to participate in the trial?

If you decide to participate in the experimentation, you will be randomly assigned to one of the three different groups that will be formed during the experimentation: The first group will be subjected to 3 cycles of a low-calorie diet (one cycle every three months) for the duration of six months ; the second group will be subjected to the low-calorie diet in combination with the longevity diet for a period of six months; the third group will continue the usual diet side by side. Once the treatment is complete, participants in the control group will be given the option on a voluntary basis to undergo the longevity diet and will be followed for up to an additional six months. The duration of the project will be 18 months, but the participation in the project for each participant will be 6 months, extendable to 12 only for the subjects of the control arm who decide to undergo the optional nutritional interventions at the end of the 6 months. During the study period, the patient will be asked to provide a peripheral blood sample on which to carry out clinical and molecular investigations. Before taking part in the trial, your

doctor will ask you to perform some tests and check if you have the characteristics required to take part in it. During the trial there are no planned invasive procedures (e.g. biopsies, bone marrow sampling, etc.).

The entire program of visits and examinations foreseen during the trial is reported in the next section "What examinations, tests and procedures are foreseen in the trial?"

- What are the risks and benefits if I participate in the trial?

Participation in this trial may result in both risks and benefits. It is important to evaluate them carefully before deciding.

Expected benefits

1) *By joining the trial, you will have the opportunity to undergo two different nutritional interventions. The first is based on a balanced low-calorie diet, while the second is based on the longevity diet in combination with the low-calorie diet. Such nutritional interventions could improve your general health with a reduction in fat mass, blood pressure, markers of inflammation and a reduction in your biological age.*
2) *By joining the trial, it will contribute to the development of knowledge on the effects of low-calorie diets and longevity on human health. These diets, in fact, could have beneficial effects on your and population's health by slowing / reducing the adverse effects on human health of already known risk factors (hypertension, body mass index, inflammation) for human aging.*

Any effects of both the balanced low-calorie diet and longevity in slowing the aging process will be measured by comparing three different groups that will be formed during the trial. The first group will be subjected to 3 cycles of a low-calorie diet (one cycle every three months) for the duration of 6 months; the second group will undergo 3 cycles of a low-calorie diet in combination with the longevity diet for 6 months; the third group will continue the usual diet side by side. Once the treatment is complete, participants in the control group will be given the option on a voluntary basis to undergo the longevity diet and will be followed for up to an additional 6 months. The duration of the project will be 18 months, but the participation in the project for each participant will be 6 months, extendable to 12 only for the subjects of the control arm who decide to undergo the optional nutritional interventions at the end of the 6 months. During the study period, participants will be asked to provide a peripheral blood sample on which to carry out clinical and molecular-genetic investigations. 501 randomized participants in the three arms in a 1: 1: 1 ratio who meet specific inclusion / exclusion criteria will be enrolled in the study. The assignment to one of the three groups will occur randomly.

Potential Risks

We want to make sure that you understand immediately what some possible risks are: additional information can be found in the next section "What risks can I face if I participate in this trial"?
There are risks and inconveniences associated with the fasting mimicking diet, such as hunger, sleepiness, dizziness, headache, body aches, fatigue, low blood pressure, and, in rare cases, fainting. These dietary interventions can also cause abnormal heart rhythms, short-term nutrient deficiencies, and a weakened immune response. A long period of low-calorie diet can be especially dangerous in people who are already malnourished. There are also the risks and inconveniences associated with any allergies / intolerances to foods present in the diet (not known before participation in the study).
During the diet period, participants should drink adequate water to prevent dehydration and avoid strenuous activities / exercises. Participants should avoid using motor vehicles and heavy machinery. Participants should avoid exposure to high-temperature environments, such as hot showers or baths, and avoid alcohol consumption.
Participants should contact the investigator, consult a personal physician, or seek immediate medical help if they have any questions regarding the clinical trial or in case of necessity. At the end of the diet, participants should

gradually resume their normal diet, starting with liquid foods, such as soups and fruit juices, accompanied by light meals.
The risks and inconveniences associated with the longevity diet are very rare but could include episodes of allergies / intolerances to foods in the diet not known prior to study participation.

Participants may feel lightheaded by the blood draw. In rare events, participants may experience bruising, excessive bleeding, infection, dizziness, and fainting. Participants can stop the blood draw procedure at any time. Participants should contact their personal physician or seek immediate medical attention if bleeding and infections related to the blood draw occur.

- Is the consent final? Can I decide to withdraw from the clinical trial (voluntary exit)?

You can decide to withdraw from the trial at any time and for any reason, without having to give reasons for your decision. If you decide not to participate anymore, let one of the investigating doctors know as soon as possible: it is important to suspend treatment safely. The doctor may consider a final check-up / examination to be appropriate.

Your doctor will keep you informed of any changes in the trial that may affect your willingness to participate.

- Are there any reasons why the trial could be stopped not by my will (early termination)?

Yes, the investigating physician may decide to terminate your participation in the trial if:

***-** Your health conditions were to change and participate in the trial proves potentially harmful*

- New information became available and experimentation was no longer in your best interest

- You did not follow the agreed rules for participation in the trial

- For women: she happened to become pregnant during the experiment

-** The trial was stopped by the competent authorities or by the promoter**.

IN ANY CASE, EXPRESS THE NEED / OPPORTUNITY TO CONTINUE THE SCHEDULED FOLLOW-UP VISITS IN THE EVENT OF WITHDRAWAL OF CONSENT, SUSPENSION OF TRIAL, PREGNANCY OR OTHERWISE.

INFORMATION SECTION. FURTHER INFORMATION

1. What is the purpose of the experiment? (No more than ½ page)

With the increase in life expectancy that has affected Western countries over the last century, aging in good health is an important goal for public health. Fifteen years of extensive preclinical and clinical studies sponsored by the National Institutes of Health (NIH) and conducted at the Longevity Institute and the University of Southern California (USC) Diabetes and Obesity Research Institute have led to the development of two very promising dietary interventions effective in slow down the process of human aging longevity, but also in improving the quality of life: the Fasting Mimicking Diet (FMD) and the Longevity Diet (LD).
The objective of the study is to determine the effects of these two different dietary interventions, on body composition and cardiovascular (CV) biomarkers (body weight, BMI, blood pressure, serum lipid levels and blood dysglycemia measurements), on blood markers, biological aging, reduce the use of hypoglycaemic or antihypertensive drugs and improve the quality of sleep.

2. What are the patient groups compared? What is the intervention being tested? (no more than 1 page if there is no pattern, otherwise 1 page + 1 page for the pattern)

If you decide to participate in the experimentation, you will be randomly assigned to one of the three different groups that will be formed during the experimentation: the first group will be subjected to 3 cycles of a low-calorie diet (one cycle every three months) for the duration of 6 months; the second group will undergo 3 cycles of a low-calorie diet in combination with the longevity diet for 6 months; the third group will continue the usual diet side by side. Once the treatment is complete, participants in the control group will be given the option on a voluntary basis to undergo the longevity diet and will be followed for up to an additional 6 months. The duration of the project will be 18 months, but the participation in the project for each participant will be 6 months, extendable to 12 only for the subjects of the control arm who decide to undergo the optional nutritional interventions at the end of the 6 months. During the study period, participants will be asked to provide a peripheral blood sample on which to carry out clinical and molecular-genetic investigations. 501 randomized participants in the three arms will be enrolled in a 1: 1: 1 ratio who meet the following inclusion / exclusion criteria.

INCLUSION CRITERIA

- *Healthy volunteers*
- *Age between 30 and 65 years.*
- *Body Mass Index>= 25 kg / m2*
- *Ability to provide informed consent*

And at least one of the following parameters

- *Body Mass Index>=30 kg / m2*
- *HbA1C greater than 5.6% (or 38 mmol/mol);*
- *IGF-1 level greater than 200 ngml-1;*
- *systolic blood pressure> 130 mmHg and diastolic blood pressure> 90 mmHg; the inclusion of individuals currently taking antihypertensive medications is allowed. In this last case a careful attention will have to be paid to the self-monitoring of blood pressure during the FMD cycles;*
- *triglycerides> 150 mgdl-1;*
- *C-reactive protein> 1 mgL-1;*
- *total cholesterol> 190 mgdL-1 and LDL cholesterol> 129 mgdL-1.*

3.1.2. EXCLUSION CRITERIA

- *Individuals with a family member already included in the study;*
- *Individuals allergic to nuts (macadamia, cashews, almonds, pecans), soy, oats, sesame or celery / celeriac;*
- *pregnant women;*
- *women in a state of breastfeeding*
- *any documented cancer diagnosis within the past 5 years;*
- *any documented myocardial infarction within the past 5 years;*

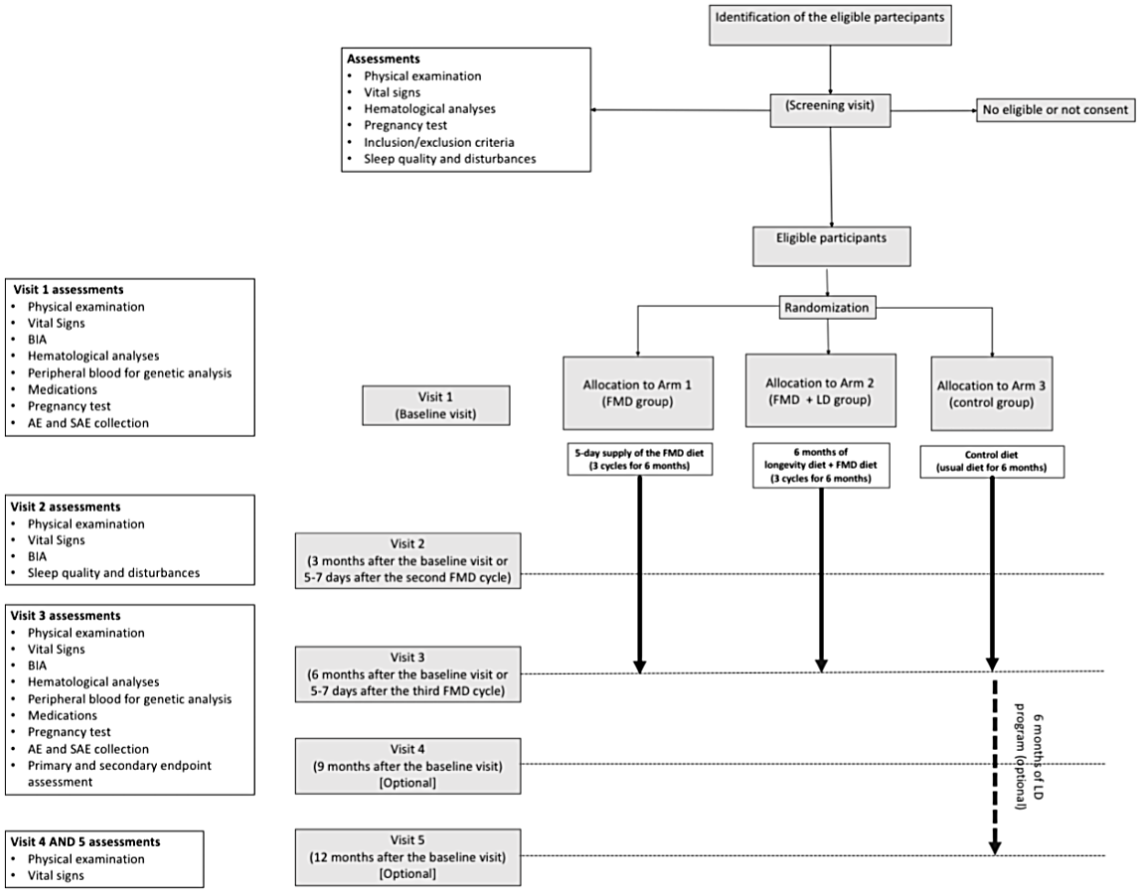
• cerebrovascular event documented in the last 5 years;
• chronic use of steroids (more than 45 consecutive days);
• insulin-dependent diabetes mellitus;
• subjects taking insulin or insulin-like drugs and subjects taking hypoglycemic agents other than metformin. In this case, close attention will therefore be paid to the self-monitoring of blood glucose during the FMD cycles;
• Individuals with severe hypertension (systolic greater than 200 mmHg and / or diastolic greater than 105 mmHg.
• Change in prescription medications, over-the-counter (OTC) medications, medical foods, and dietary supplements within 30 days prior to initiation and for the duration of the study.
• Use of drugs classified as narcotics 15 days prior to initiation and for the duration of the study.
• Use of prescription drugs and / or over-the-counter drugs for acute and semi-acute medical conditions 15 days prior to initiation and for the duration of the study. The use of paracetamol is allowed on an as-needed basis.
• Use of an investigational drug or participation in an investigational study within 30 days prior to initiation and for the duration of the study.
• Use of oral or injectable corticosteroids within 30 days prior to initiation and for the duration of the study.
• Use of anticoagulant medications (heparin compounds or warfarin) within 30 days prior to initiation and for the duration of the study. It is allowed to use aspirin 81 mg or 325 mg once a day.
• Use of prescription neuroactive drugs, including major and atypical antipsychotic drugs, antidepressants, anxiolytics, and epilepsy drugs within 30 days prior to initiation and for the duration of the study.
• Participants will not be allowed to stop prescribed drugs to meet the entry criteria.
• A history of allergy or intolerance to the food products used in the study. Detailed descriptions of the study product are included in Section 4.1 and 4.2 of the study protocol and attached to the Study Informed Consent.
• Clinically significant vital signs abnormalities (systolic blood pressure <90 mmHg or> 200 mmHg, diastolic blood pressure <50 mmHg or> 105 mmHg or resting heart rate <50 or> 100 bpm) at the screening visit.
• A severe and unstable disease which includes heart, liver, kidney, gastrointestinal, respiratory, endocrinological, neurological, immunological, or hematological disease.
• Known HIV infection, tuberculosis or hepatitis B or C.
• A current diagnosis or personal history of:
    - any cardiovascular disease including myocardial infarction, angina, cardiovascular surgery (within 5 years), congestive heart failure, cardiac arrhythmias or conduction abnormalities, cerebrovascular accident, transient ischemic attack (TIA) or peripheral vascular disease, deep vein thrombosis or pulmonary embolism. Diabetes mellitus requiring inhaled or injected insulin.
    - Any autoimmune disease such as inflammatory bowel disease (including Crohn's disease and / or ulcerative colitis), multiple sclerosis, rheumatoid arthritis, systemic lupus erythematosus, polymyositis, scleroderma and / or thyroiditis.
    - Any significant liver or kidney disease such as cirrhosis or non-alcoholic fatty liver disease, glomerulonephritis and / or ongoing dialysis treatment.
    - Any malignancy (except adequately treated malignancies with no known recurrence for> 2 years).
    - Any severe mental illness including a history of attempted suicide.
• Use of drugs (such as marijuana, cocaine, phencyclidine [PCP] and methamphetamine) 15 days before the start of the study and for the duration of the study.
• History of regular consumption of> 14 alcoholic drinks per week for women and> 21 drinks per week for men (1 drink = 35cl of beer, 12cl of wine or 30ml of spirits).
• Any conditions in which bioelectrical impedance testing would be impossible or uninterpretable (e.g. prosthetic extremities on both sides, limb amputation, implanted pacemaker, inability to lay still or supine, or skin defects on preferred electrode placemen sites.
• Inability to comply with the study and / or follow-up visits.
• Any concomitant conditions (including clinically significant abnormalities in medical history, physical examination, or laboratory evaluations) that, in the PI's opinion, would preclude safe participation in this study or interfere with compliance.

• Any valid medical, psychiatric and / or social reasons that, in the opinion of the PI, would preclude safe participation in this study or interfere with compliance.
• Abnormal laboratory reports including: abnormal blood count (hematocrit <33% or> 47%; white blood cells <3.0 or> 12.0 x10^3 / mm3; platelets <140 or> 500 x 10^9 / l); abnormal kidney function test (creatinine> 2.5 mg / dL) or liver function test (AST, ALT, alkaline phosphatase)> 1.5 times the upper limit of normal; serum calcium> 11 mg / dL); Serum K <3.5 mEq / L; Na <134 or> 148 mmolL^-1.

The nutritional interventions to which you may be subjected to are a fasting mimicking diet or a longevity diet. The fasting mimicking diet, to be repeated every 3 months, consists of a food protocol scheduled over 5 consecutive days designed to implement a simulated fast. This program aims to encourage the conduct of a healthier diet thanks to which the effect of risk factors in cardio-metabolic and chronic-degenerative diseases can be reduced. This food program provides about 1100 kcal in the first day of the diet and about 800 kcal from the second to the fifth day of the diet. It includes several components formulated with organic ingredients including bars, olives, soups, drinks, and supplements, entirely vegetable, gluten, and lactose free. The kit developed to implement this food program in a simple and practical way is divided into five small boxes, one for each diet day. Specifically, the nutritional composition is divided into about 45% of carbohydrates, of which 9% are simple, about 45% lipids, mainly unsaturated and 9-10% of vegetable proteins. From the 2nd to the 5th day of the fasting mimicking diet there is a vegetable glycerin-based drink that must be diluted according to body weight, as per the indicator label. All the instructions are found inside the Diet Card provided inside the box.

The longevity diet, on the other hand, appears to have as its basis the nutrition of the longest-lived centenarians in the world, but thanks to scientific evidence, the tests and the results achieved, the basic principles have been developed. It is a diet that comes as close as possible to a vegetarian-like diet (legumes, vegetables, fruit) and fish, limiting fish to 2-3 times a week and avoiding fish that contain high percentages of mercury (swordfish, tuna) in which the daily protein intake must be around 0.7-0.8 g / kg of body weight to be increased slightly after the age of 65. It is essential to consume meals within 12 hours or less a day (starting after 8 and ending before 20, or before 21) with a preference for complex carbohydrates (tomatoes, broccoli, legumes, carrots, legumes, whole meal bread, etc.) and good fats, minimizing saturated fats and simple sugars; at the base of a good diet there must be a good quantity of good unsaturated fats such as mono- and poly-unsaturated fats of quality such as those present in fatty fish (salmon, mackerel, sardines), in dark chocolate> 85%, in nuts (almonds, walnuts, etc.) and in extra virgin olive oil and low in saturated hydrogenated and trans fats. The Longevity Diet is not just a dietary scheme, but an approach to be followed for all the inhabitants of the world; most long-term diets are abandoned by patients, either because they are too restrictive and not very satiating or because they require too radical a change in a person's lifestyle. This dietary approach, on the other hand, turns out to be easily applicable, having as a basis many points in common with the Mediterranean Diet and allows you to eat more and not less.

Clinical trial design



3. What examinations, tests and procedures are foreseen if I participate in the trial? (Section no longer than ¾ page, unless many exams / procedures are foreseen)

If you decide to participate in the experimentation, you will be randomly assigned to one of the three different groups that will be formed during the experimentation. Regardless of the group to which I will be assigned, will undergo 5 medical examinations: the pre screening visit (by telephone), the enrollment visit, the baseline visit, a visit at 3 and 6 months from the beginning of the nutritional intervention (fasting-mimicking diet or longevity diet) and two optional visit at 9 months and 12 months after the conclusion of the nutritional intervention if it will be assigned to the control group. If you decide to participate in the trial, you will be provided with a schedule of visits with the exams to be done, which will be booked directly by the center. During these visits, the following will be carried out:

- bioimpedance analysis for the study of body composition;

- evaluation of vital parameters including blood pressure;

- venous blood sampling which will include fasting glucose, glycated hemoglobin, lipid profile, C-reactive protein, creatinine, IGF-1, IGFBP3, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, homocysteine, and complete blood count.

- Telomere length on DNA extracted from peripheral blood by RT-PCR.

The blood samples, about 25 ml for each visit, will be used both for hematological analyzes and as a source for DNA extraction

The exams will be carried out in collaboration with the University of Palermo and the IFOM-FIRC Institute of Molecular Oncology Foundation of Milan. The sharing of samples will take place through couriers in compliance with current regulations in terms of privacy, sample identification and transport (IATA sample shipping management).

4. What risks can I face if I participate in the trial? *(Section no longer than 4 pages)*

There are risks and discomforts associated with the fasting mimicking diet, such as hunger, anxiety, drowsiness, dizziness, headache, body aches, fatigue, low blood pressure and, in rare cases, fainting. These dietary interventions can also cause abnormal heart rhythms, short-term nutrient deficiencies, and a weakened immune response. A long period of a low-calorie diet can be particularly dangerous in people who are already malnourished. There are also the risks and inconveniences associated with any allergies / intolerances to foods present in the diet (not known before participation in the study).
During the diet period, participants should drink adequate water to prevent dehydration and avoid strenuous activities / exercises. Participants should avoid using motor vehicles and heavy machinery. Participants should avoid exposure to high-temperature environments, such as hot showers or baths, and avoid alcohol consumption.
Participants should contact the investigator, consult a personal physician, or seek immediate medical help if they have any questions regarding or feel discomfort.
At the end of the diet, participants should gradually resume their normal diet, starting with liquid foods, such as soups and fruit juices, accompanied by light meals.
The risks and inconveniences associated with the longevity diet are very rare but could include episodes of allergies / intolerances to foods in the diet not known prior to study participation.
Participants may feel lightheaded by the blood draw. In rare events, participants may experience bruising, excessive bleeding, infection, dizziness, and fainting. Participants can stop the blood draw procedure at any time. Participants should contact their personal physician or seek immediate medical attention if bleeding and infections related to the blood draw occur.

5. What information should I know about contraception and pregnancy?

You must agree not to become pregnant or conceive a child while participating in this study. It is mandatory to use an appropriate method of contraception. Such methods include total abstinence, female sterilization, male sterilization, or use of oral / injectable / implantable contraceptives.

Contraception (including abstinence from sexual intercourse) is required because it is not known whether the study treatment can cause harm to the fetus. Tell your study doctor or your team immediately if you think you may be pregnant or have conceived a baby before receiving any further study treatments.

6. How will you be notified of any unexpected results following diagnostic investigations?

IN THE CURRENT STATE OF KNOWLEDGE, INCLUDING THAT RELATING TO EPIGENETIC WATCHES, FROM THE PERFORMANCE OF THE ANALYSIS PROVIDED BY THE EXPERIMENTATION, NO RESULTS RELATING YOUR SUSCEPTIBILITY TO DEVELOPE PARTICULAR DISEASES OR TO BE CARRIER OF GENETIC ILLNESSES, THAT COULD POTENTIALLY LEAD TO THE BIRTH OF SICK CHILDREN.

7. Is it useful / necessary to inform my family doctor?

In consideration of the design of the trial, if you decide to participate, it is important to inform your general practitioner. To this end, we have prepared a letter that you will be able to deliver to him, in which the procedures of the trial are explained.

8. What will my commitment be and what will my responsibilities be if I decide to participate? (section no longer than ½ page)

- *Scrupulously observe the indications and requests from the health personnel following the trial and ensure attendance at appointments.*
- *Inform the doctor following the trial:*

or *of all drugs you are taking including drugs from unconventional medicine;*
or *any side effect that arises during the trial;*

or *any visit to or hospitalization in facilities other than the trial center;*
or *current or previous participation in other clinical trials.*
or *avoid pregnancy or breastfeeding during the trial.*

9. Will I have to face costs for participating in the trial? Will I be reimbursed for any expenses? Will I get paid?

There are no costs for you deriving from participation in the trial as these are fully covered by the Sponsor. There is also no financial compensation for participation in the trial.

10. What happens if I suffer damage because of participating in the trial?

Participation in a clinical trial may involve drawbacks and risks that cannot be determined prior. For this reason, the clinical trial provides insurance coverage to protect your participation.

In compliance with the laws, insurance is provided to cover any damage suffered due to participation in the trial, for the entire period of the same, to cover the civil liability of the investigator and promoter.

INSURANCE COMPANY: LLOYD'S; MAXIMUM PER PARTICIPANT 1,000,000; MAXIMUM AGGREGATE: 5,000,000; *the details are attached*

It should be noted that, according to the Ministerial Decree of 14 July 2009, the insurance policy does not cover the value exceeding the ceiling and is effective exclusively for damages whose compensation request has been submitted no later than the period provided for in the policy (36 MONTHS). However, this limitation does not affect your right to obtain compensation from the person responsible for any damage (to protect the subject of the trial).

11. How will they be treated and who will have access to my health data, including identification data, during the trial?

Your data, personal and health data and only to the extent that they are indispensable in relation to the objective of the trial and for pharmacovigilance purposes, will be processed in compliance with the 2016/679 EU Regulation, known as GDPR (General Data Protection Regulation) and of the Legislative Decree 10 August 2018, n. 101. In practical terms, the documents relating to the participant will be kept in a safe place and will not bear his name in clear text, known only to the researchers, but an identification code.

The data, made anonymous, may be subject to control by regulatory bodies and used for scientific publications (journals, conferences).

Your clinical data collected for the purposes of the trial, as well as the results of the tests performed, will be kept for a maximum period of 15 years, and subsequently destroyed. They will not be destroyed only if a) it is no longer possible to trace them back to its identity, because they are anonymized during the trial itself; b) in the presence of your specific informed consent.

If personal data are transferred to a third country or to an international organization, all the guarantees provided for by article 46 of the GDPR 679/2016 relating to the transfer will be adopted.

Further information is included in the attached data processing authorization form.

12. How will they be treated and who will have access to my biological samples taken for the purposes of the experiment?

As for your health data, also your biological samples, pseudonymized (a technique that allows you to modify and mask the personal and sensitive data of a natural person, in order not to make them directly and easily attributable to the same), will be used for of experimentation.

Once the experimentation is complete, its samples will be labeled with a numerical code and stored at -80 ° C in the Genetics laboratory of the University of Calabria. Access to samples and data will be reserved only for the

staff involved in the study. With this form we are also asking you an authorization to keep your DNA samples for a maximum of 15 years from the end of the study, for future research on the aging process. In this case, the opinion of the Ethics Committee on the new genetic research studies will be requested.

13. How will I have access to the results of the trial?

Once the experimentation has been completed and all the resulting data collected, they will be analyzed to draw conclusions. The investigators and the promoter undertake to make them available to the scientific community.

The law provides for the possibility of access for participants to the results of the experimentation. Therefore, you can ask the investigating physician to tell you the general results of the trial

14. Has the trial been approved by the Ethics Committee?

The trial protocol that was proposed to you was examined and approved by the Ethics Committee of the University of Calabria. Among other things, the Ethics Committee verified the compliance of the trial with the Rules of Good Clinical Practice and the ethical principles expressed in the Declaration of Helsinki and that your safety, rights, and your well-being have been protected.

15. Who can I refer to for more information on the clinical trial I am invited to participate in?

DR. ROMINA INÈS CERVIGNI
SCIENTIFIC MANAGER OF VALTER LONGO ONLUS FOUNDATION
MILAN, LOMBARDY, ITALY
TEL. 3397805607

PROF. VALTER LONGO
IFOM- FIRC INSTITUTE OF MOLECULAR ONCOLOGY FOUNDATION
MILAN, LOMBARDY, ITALY
TEL. 02574303801

PROF. ALBERTO MONTESANTO
GENETICS LABORATORY, UNIVERSITY OF CALABRIA,
VIA P. BUCCI, CUBO BUILDING 6 / C - 1st FLOOR ARCAVACATA DI RENDE (CS).
TEL. 0984492901

10. If I join the trial, who can I contact in case of need?

For any doubt and non-programmable or unscheduled event during the trial (doubts relating to the treatment in progress, side effects, decision to abandon the trial, etc.), you can contact:

DR. SSA ROMINA INÈS CERVIGNI
SCIENTIFIC MANAGER OF VALTER LONGO ONLUS FOUNDATION
MILAN, LOMBARDY, ITALY
TEL. 3397805607

PROF. VALTER LONGO
IFOM- FIRC INSTITUTE OF MOLECULAR ONCOLOGY FOUNDATION
MILAN, LOMBARDY, ITALY
TEL. 02574303801

DR. ALBERTO MONTESANTO
GENETICS LABORATORY, UNIVERSITY OF CALABRIA,
VIA P. BUCCI, CUBO BUILDING 6 / C - 1st FLOOR ARCAVACATA DI RENDE (CS).
TEL. 0984492901

*If you consider it appropriate to report events or facts relating to the trial which you have joined to people not directly involved in the trial itself, you can refer to the INRCA Ethics Committee which approved the trial.*_____ ___/___/_____ _____ _____

Full name of the doctor who delivered the information | Date | hour | signature

Attachments

- Insurance policy
- Form for consent for processing personal data
- Fasting mimicking diet nutritional sheet.
- Fasting mimicking diet food program.
- Longevity diet diet food program.
- Blood tests list

Additional documents:

- Letter to the doctor.

D. EXPRESSION OF CONSENT SECTION

(Notes: 1 copy for the participant, 1 copy for the trial manager)

Title of the trial: _____ _____

Protocol code, version, and date: _____

Promoter of the trial / sponsor / funding body: Calabria Region_____

Principal Investigator (NAME, AFFILIATION, REFERENCES): ROMINA INÈS CERVIGNI

I, the undersigned _____

born in _____ on ___/___/_____

I DECLARE

☐ that I have received from Doctor _____ detailed explanations regarding the request for participation in the research in question, as reported in the information section, forming part of this consent, of which I was given a copy on _____ at _____ (indicate date and time of delivery);

☐ that they have been clearly explained to me and I have understood the nature, the purposes, the procedures, the expected benefits, the risks and possible inconveniences and the alternative treatment modalities with respect to the proposed clinical trial;

☐ to have had the opportunity to ask any question to the investigator of the study and to have received satisfactory answers;

☐ that you have had sufficient time to reflect on the information received;

☐ that you have had sufficient time to discuss it with third parties;

☐ to have been informed that the trial protocol and all the modules used have had the favorable opinion of the competent Ethical Committee;

☐ to be aware that the research can be interrupted at any time, by decision of the research manager;

☐ that I have been informed that I will be made aware of any new data that could compromise the safety of the research and that, for any problem or further questions, I will be able to contact the doctors where I am being treated;

☐ that for the best protection of my health I am aware of the importance (and my responsibility) of informing the general practitioner of the trial in which I agree to participate. I am aware of the importance of providing all information (drugs, side effects, etc.) concerning me to the investigator;

☐ that I have been informed that the results will be disclosed to the scientific community, protecting my identity according to the current legislation on privacy;

☐ to be aware that any choice expressed in this consent form may be revoked at any time and without any justification;

☐ that I have received a copy of this consent form.

I therefore DECLARE to

☐ YES		participate in the experimentation
☐ YES	☐ NO	be informed of all unexpected news relating to my present or future health that may accidently emerge from the investigations envisaged by the trial, including genetic ones, when this may entail possible benefits.
☐ YES	☐ NO	be informed of unexpected news relating to my present or future health only when it will be useful for my health care or to allow me to make informed reproductive choices
☐ YES	☐ NO	be contacted after the end of the trial to provide information on my state of health (applies only to contacts not foreseen as a follow-up to the study protocol)
if applicable:		
☐ YES	☐ NO	the use of contraceptive drugs

_____	___/___/_____	_____	_____
Full name of the adult patient	Date	hour	Signature
_____	___/___/_____	_____	_____
Full name of legal representative	Date	hour	Signature

STATEMENT BY THE DOCTOR WHO GETS THE CONSENT

_____

(Patient name, place, and date of birth)

Title of the trial: _____

Protocol code, version, and date: _____

Promoter of the trial / sponsor: _____

Principal Investigator (NAME, AFFILIATION, REFERENCES): _____

_____

I, the undersigned Prof./Dr…… …… in my capacity as Investigator
Last name First name
principal (or delegate of the principal investigator)

I DECLARE

that the Patient has voluntarily consented to his participation in the trial

I also declare that:

- ☐ have provided the Patient with comprehensive explanations regarding the purpose of the trial, the procedures, the possible risks and benefits and its possible alternatives;
- ☐ having verified that the patient has sufficiently understood the information provided
- ☐ having given the patient the necessary time and the opportunity to ask questions about the trial
- ☐ to have clearly illustrated the possibility of withdrawing from the trial at any time or of changing the choices made
- ☐ not having exercised any coercion or undue influence in requesting this consent
- ☐ have provided the patient with information on how the results of the trial will be disclosed to him / her

_____ _____
Place and Date Hour

_____

_____

Name Surname (block letters) of the doctor who provided the Signature (and stamp)

information and who has collected consent

This form is an integral part and must be kept together

to the information form for informed consent