Double-blind, randomized, parallel-group, monocentric, placebo-controlled cross-over clinical trial on the effect of a food supplement based on S-adenosyl methionine and probiotics to promote normal mood by reducing subthreshold depression as a risk factor for major depression

INFORMATION SHEET
and
INFORMED CONSENT

Proposal for the use of food supplement based on S-adenosyl methionine and probiotics to promote normal mood in different clinical settings

Dear Sir
the Ethics Committee (EC) gave a positive opinion to conduct a scientific study on the effects of a food supplements based on S-adenosyl methionine (SAMe) and probiotics, an ingredient legally approved in food supplements by Italian Legislation, used to have beneficial effects on mood. In order to carry out this study, we need the cooperation of people like you, that have the right characteristics for the clinical trial that we will explain to you.
So that you can give a possible consent to participate in the study, it is important that you understand the purpose of this study and what a possible participation (in terms of benefits, risks and inconveniences, due to the necessity to follow accurately the procedures, specified inside the protocol) will lead to you.
We ask you to read this document and, if you wish, you can take all the time that you need to discuss about it with your family and with your own doctor. We invite you to ask for any explanation if the information supplied to you are not clear or if you need any kind of clarifications.

REASONS AND OBJECTIVES THAT THE STUDY AIMS TO REACH

This study aims to define the effects of a food supplement containing SAMe and probiotics on mood.
In particular, the monitoring of the effects after the intake of the food supplement based on SAMe and probiotics regarding mood will be evaluated by validated questionnaires, such as Patient Health Questionnaire-9 (PHQ-9) and Hamilton Depression Rating Scale (HAMD21), and by the assessment of the effect on urinary cortisol and epinephrine concentration.

Primary outcome measure

Subthreshold depression as a risk factor for major depression, measured by the Patient Health Questionnaire-9 (PHQ-9) and Hamilton Depression Rating Scale (HAMD21) at t0, t12, t16, t28.

Secondary outcome measures
Urinary cortisol and epinephrine concentration assessed by urine analysis at t0, t12, t28.

Baseline = t0, after 12 weeks of treatment = t12, after 16 weeks (4 weeks of wash-out) = t16 and after 28 weeks of the other treatment = t28

You presents:

– Alterated mood

In an effort to get a significant improvement on mood, we propose you a treatment that uses a food supplement containing SAMe and probiotics.

PROPOSED TREATMENT

In this clinical trial, we propose the use of a **food supplement containing** SAMe and probiotics as an alternative to drugs or other food supplements**.** It is important that you know that the available data on the efficiency of food supplement used in this study, to promote a normal mood, are still limited.

The food supplement containing SAMe and probiotics or placebo will be administered according to the following regimen:
Subjects will take the food supplement or placebo daily for 3 months, then a 1-month wash-out period is planned (no treatment will be administered). Subsequently, subjects assigned to the treated group will be reassigned to the control group and vice versa (a further 3 months of treatment), as a cross-over design

We hope that the food supplement containing SAMe and probiotics would give you benefit also in your case, although we are aware that there is always a sort of variability in the individual responses. The scientific data available are too limited to be able to say that the treatment is certainly effective, or to assure you all the effects.

The Ethics Committee of the ASL of Caserta (Campania Nord) has previously assessed and authorized what we're proposing you today.

RISKS AND SIDE EFFECTS

The subjects will be monitored diligently and, in case of side effects during the study, the subject will suspend the consumption of the food supplements and the same will ends the study.
The safety will be evaluated by reports of suspected AEs collected within the form based on the schedule used by of the Italian National Institute of Health, Ministry of Health (www.vigierbe.it), and by the determination of a possible hepatic and/or renal toxicity

POSSIBLE BENEFITS TO PARTICIPATE TO THE CLINICAL TRIAL

Participants taking part in this study may have a benefit on mood. Subjects will be continuously monitored during the entire study.

FREE CHOICE TO PARTICIPATE TO THE CLINICAL TRIAL

The decision to participate to the project or is completely up to you. If you decide to participate, we will provide you the informed consent that you have to sign.
The possible participation will be covered by an insurance policy (n ._____ and valid until _____).

IF YOU DECIDES TO NOT TAKE PART OR TO INTERRUPT THE STUDY

If you choose to not take part or to interrupt the study, you can do it freely warning the investigator, without giving any justification and without changing your health care in this centre.
Similarly, always in yours interest, the test may be interrupted, if the principal doctor believe that the treatment is not good for you or if there are some undesirable and / or unpredictable effects.
In this case you will be immediately informed of your state of health and possible treatments available to restore it.

INVESTIGATIONS REQUIRED FOR PARTICIPATION TO THE STUDY

If you agree to participate to this study, you will do a first visit to verify if you can be part of this study.

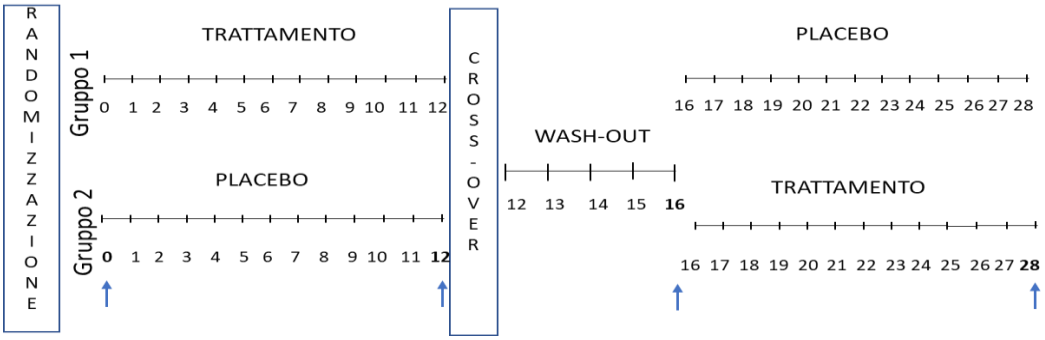

Figure 1. Type of study adopted

EXPENDITURE RELATIVE TO THE STUDY.

From participation to this study there will be any costs for you and the food supplements will be free.

CONTACT PERSONS

If you have any problems or questions, the medical investigator is at your disposal and he can be contacted as follows:
Name of the Medical Investigator_____
Phone _____

This document about the clinical trial was prepared in accordance with standards of Good Clinical Practice of the European Union and the current revision of the Declaration of Helsinki, and was approved by the ASL Caserta Campania Nord Ethics Committee (Via Unità Italiana, n28, 81100, Caserta, Italy; +39 (0)825203025; comitatoeticoav@agmail.it), which you can contact to report any kind of event that you see.

We left you all the time that you need to evaluate all the information and to ask any kind of explanations.

And you will receive a copy of the information sheet and informed consent signed by the doctor.

DECLARATION OF CONSENT AND SIGNATURE

I, the undersigned (full name) _____

_____ Age Sex M F birth date __ / __ / __

Address: Street / _____
Square

CAP _____ City _____

tel _____

I certify that:

participate voluntarily in the study: "**Double-blind, randomized, parallel-group, monocentric, placebo-controlled cross-over clinical trial on the effect of a food supplement based on S-adenosyl methionine and probiotics to promote normal mood by reducing subthreshold depression as a risk factor for major depression**" with the aim to define the effects of a food supplement containing SAMe and probiotics on mood in the absence of other food supplements for mood conditions at the time of recruitment and in the previous two weeks.

- I received from the investigator Doctor all the information in a clear and comprehensive way on the purposes and procedures of the trial;
- I have read and understood the information sheet that was handed to me early enough and that confirms what they have been told me verbally;
- I had the opportunity to ask clarification and satisfactory answers, as well as to have had the opportunity to discuss the details of the study with a trusted person;
- being inform to the results that I gain and the risks or reasonably expected disruption, and to have had enough time to decide
- be aware:
    - that be part of this study is a voluntary decision and I can left the study of my own free will without giving reasons, having received the assurance that leave the clinical study will not have any effects on my health care in future;
    - that my clinical data could be examined or used for scientific publications, but will remain strictly confidential in accordance with the local regulations and the subsequent amendments and additions;

  - that the Ethics Committee ASL of Caserta (of which I have the phone number) approved the experimental protocol of the study;
  - I'll be made aware, during the trial, about any new data that may compromise the security of the food supplement and the method of treatment;
  - Aware of my rights to have free access to the documentation concerning to the trial (insurance, clinical-scientific, drug-therapy) and to the assessment made by the Ethics Committee, who I could contact if desire;
- which it was signed an Insurance Policy in favour of the subjects being part of the study for any damages with the society insurer _____with a maxime compensation;
- having to sign two identical modules of this informed consent: the original one will be preserved by the investigator (and stored for at least 15 years) and the second one will be delivered to me;
- I'll have to contact for any type of problems or for additional information to:
- Dr./prof. _____
  Address_____
  Phone _____
- that in my interest the investigator will decide my exclusion from the study.
- I express my consent to the processing of my personal data for statistical purposes in accordance with Regulation (EU) 2016/679.

Therefore I freely agree to be part in this study.
The signature on this document will not have any effect on my legal rights.

_____ _____

Signature of the person who is included into the study Date

I declare that I have explained in a complete and exhaustive way the aspects of this treatment to the patient and / or to the person who's authorized to give consent to the patient's name.

_____ _____ _____

Signature of Medical Director Name and Surname Date