PATIENT INFORMED CONSENT

STUDY TITLE: Immune Boosting with Zinc Supplements to Reduce Inflammation, Viral Load, and Mortality in COVID-19 Infection.

VERSION AND DATE: Version 1.0, February 12, 2021.
PROMOTER: Consorci Mar Parc de Salut de Barcelona (Parc de Salut Mar). Passeig Marítim 25-29, 08003, Barcelona.
PRINCIPAL INVESTIGATOR: Robert Güerri-Fernández & Silvia Gómez-Zorrilla Martín
CENTER : Hospital del Mar

INTRODUCTION

We are writing to inform you about a research study in which you are invited to participate. The study has been approved by a Drug Research Ethics Committee. The study will be carried out in accordance with the Standards of Good Clinical Practice and will respect the Declaration of Helsinki (October 2013 version, Fortaleza, Brazil). Our intention is only that you receive correct and sufficient information so that you can decide whether or not to participate in this study. To do this, read this information sheet carefully and we will clarify any doubts that may arise after the explanation.

VOLUNTARY PARTICIPATION

You should be aware that your participation in this study is voluntary and that you may decide not to participate or change your decision and withdraw consent at any time, without altering your relationship with your doctor or affecting your health care.

THE PURPOSE OF THE STUDY

Zinc is an essential element of nutrition that is present in many foods. It is an essential mineral for health with several functions, including participating in the immune system. Zinc deficiency situations have been associated with an increased risk of infectious diseases. Furthermore, zinc has been shown to have direct antiviral activity against several viruses, including the of the families of the rhinovirus and coronavirus. He aim of this study

is to determine if dietary zinc supplementation in patients with COVID-19 infection could decrease the severity of the infection, by attenuating the inflammation produced by the virus and the viral load. Therefore, it is expected that zinc supplementation can help improve the clinical status of patients with Covid-19 infection and their evolution.

STUDY DESCRIPTION

Adult patients admitted to the Hospital del Mar with COVID-19 infection will participate in this study. A total of 60 patients are expected to participate. If you decide to participate in the study, you will be asked to sign a consent form confirming that you have understood the study and want to participate. All volunteers participating in the study will receive standard treatment for COVID-19. In addition, you will be randomly assigned by a computer program to one of the two arms of the study:

1) Receive conventional treatment according to the protocol that is administered in the hospital for COVID-19 infection

   either

2) Receive conventional treatment according to the protocol that is administered in the hospital for the COVID-19 infection and also nutritional supplements with zinc (zinc acetate supplements 80mg once a day for 14 days).

Of the 60 patients scheduled to participate in the study, 30 will receive zinc supplementation and 30 will not. In both groups, clinical management and follow-up by the responsible physician will continue to be the usual.

To carry out the study it will be necessary for us to ask a series of questions related to your state of health and illness. We will also collect data from your medical history, which will be treated confidentially and a general physical examination will be performed by the study doctors. In addition, three blood samples will be taken during the study (on the day of study inclusion, 14 days and approximately 30 days after study inclusion). In no case will 100 mL of blood be exceeded throughout the study.

STUDY ACTIVITIES

The study will be carried out during the first 28 days after the informed consent is signed. You will receive standard care and if included in

intervention group, should take the Zinc supplement once a day for the first 14 days (day 1 to 14):

- **Initial visit (Day 0):** your medical history and medication for the last month, your clinical status (vital signs, X-ray and perception of the disease) will be assessed and a blood test will be performed. A diagnostic test for Covid-19 by PCR or serology could also be done. In women of childbearing age a pregnancy test will be performed, if it is positive it will not be included in the study. Lactating women will also not be able to participate in the study. If applicable, zinc supplements will be given to you along with instructions for their use. administration.
- **Visit 2 (Day 7 ± 2):** If you are admitted, a visit will be made by a study doctor to see how you are, the evolution of the disease, how you have tolerated the supplements, if you are taking any medication and possible effects adverse. In the event that you are no longer admitted, this visit will be made by calling telephone.
- **Visit 3 (Day 14 ± 2):** Final treatment visit. This visit will be in person and a physical examination will be carried out by the study doctor, vital signs will be taken and a blood sample (20mL) will be carried out, which will help us to analyze the inflammatory response and to be able to study the efficacy of zinc supplementation. . In addition, you will be asked about the evolution of the symptoms you present, about the medication you are taking, about compliance with taking the zinc supplement where appropriate, tolerance and possible effects. adverse.
- **Visit 4 (Day 28 ± 2):** End of study visit. In-person visit in which vital signs will be taken, a physical examination will be performed by the study doctor, and a blood sample (20mL) will be performed. In addition, you will be asked about the evolution of the symptoms you present, about the medication you are taking, about compliance with taking the zinc supplement where appropriate, tolerance and possible effects. adverse.

RISKS AND DISCOMFORT DERIVED FROM YOUR PARTICIPATION IN THE STUDY

Zinc supplements can cause mild gastrointestinal discomfort such as nausea, vomiting, abdominal discomfort or diarrhea. They are usually of mild intensity and appear only during the first days. Zinc supplementation is not expected to produce any adverse effects beyond these possible abdominal discomforts.

The study requires an investment of time on their part, and the participant is expected to be responsible for following the administration regimen of the study product, answering phone calls and visits on the scheduled days, complying with study activities, notifying any adverse event that happens to you, as well as any change in your medication. Finally, during the study, some blood tests will be performed. For most people, needle sticks to draw blood are not a problem. However, on occasion, they can cause bleeding, bruising, discomfort and/or pain at the point of blood extraction. You may also feel dizzy.

BENEFITS DERIVED FROM YOUR PARTICIPATION IN THE STUDY

Zinc supplementation could be associated with a better recovery from the disease and could prevent complications. However, there may be no direct benefit to you from participating in this study. In any case, we hope to gain more knowledge about COVID-19 infection, which we hope may help other patients in the future.

WARNING RELATING TO PREGNANCY AND BREASTFEEDING.

A pregnancy test will be carried out before the beginning of the study in women of childbearing age, if it is positive, they will not be able to take part in the study. There is no literature that has shown harmful effects of zinc supplementation during pregnancy on the embryo, fetus, or mother. As for lactation, zinc is excreted through breast milk .

EXPENSES AND ECONOMIC COMPENSATION

Your participation in the study will incur no additional cost to you. You will not have to pay for the medication or study-specific tests. You will not receive any financial compensation for participating in the study. The health center and its researcher will not receive financial compensation either.

SURE.

For participation in this study you will be covered by the insurance policy of the hospital. It is not planned to contract a specific insurance.

REVOCATION OF CONSENT.

You may revoke consent once you have given it without giving any explanation, without this having any repercussions on your current or future care and without affecting the relationship with the healthcare teams that care for you.

PROTECTION OF PERSONAL DATA, DATA PROCESSING AND CONFIDENTIALITY.

Your consent is requested for the use of your data and your sample for the development of this project. Both personal data (age, sex, race), as well as health data, as well as the sample for research, will be collected using a coding procedure. Only the researcher and/or the doctor in charge of your center will be able to relate this data to you, being responsible for safeguarding the consent document, guaranteeing compliance with your will in relation to the use of the biological sample that you assign for investigation.

The information will be processed during the analysis of the results obtained and will appear in the final reports. The data will be analyzed in a grouped way, in no case will it be possible to identify you, guaranteeing the confidentiality of the information obtained, in compliance with current legislation. The transfer of data outside the EU is not foreseen. It is expected that the results of the study will be communicated at scientific meetings, national and international medical congresses, as well as published in scientific journals to share the knowledge obtained during the project with the rest of the scientific community. Your identity will always be kept strictly confidential.

The treatment, communication and transfer of personal data of all participating subjects will comply with the provisions of Organic Law 3/2018, of December 5, Protection of Personal Data and guarantee of digital rights legislation in the European Union (EU) on personal data, specifically Regulation (EU) 2016/679 of the European Parliament and of the Council of April 27, 2016 on Data Protection (RGPD). This new regulation establishes a new framework in terms of data protection. The promoter agrees to comply with it, and therefore it is important that you know the following information:

In accordance with the provisions of the aforementioned legislation, you can exercise the rights of access, modification, opposition and cancellation of data, and limit the treatment of data that is incorrect, request a copy or that it be transferred to a

third (portability) the data that you have provided for the study. To exercise your rights, contact the main researcher of the study or the Data Protection Officer of the center _____. We remind you that the data cannot be deleted, even if you stop participating in the trial to ensure the validity of the research and comply with legal duties and drug authorization requirements. Likewise, you have the right to contact the Data Protection Agency if you are not satisfied. Contact details can be found on the website: www.agpd.es .

Both the Center and the Promoter are respectively responsible for the processing of your data and undertake to comply with the data protection regulations in force. All information collected, stored and processed will be anonymous. The data collected for the study will be identified by a code, so that information that could identify you is not included, and only your study doctor/collaborators will be able to relate said data to you and your medical history. Therefore, your identity will not be revealed to any other person except the health authorities, when required or in cases of medical urgency. The Research Ethics Committees, the representatives of the Health Authority in inspection matters and the personnel authorized by the Sponsor, may only access to verify the personal data, the clinical study procedures and compliance with the standards of good clinical practice. (always maintaining the confidentiality of the information).

The Investigator and the Sponsor will keep the data collected for the study for at least 25 years after its completion. Subsequently, your personal information will only be kept by the health care center and by the sponsor for other scientific research purposes if you have given your consent to do so, and if permitted by law and ethical requirements. applicable.

If we transfer your encrypted data outside the EU to our group entities, service providers or scientific researchers who collaborate with us, the participant's data will be protected with safeguards such as contracts or other mechanisms by data protection authorities. data. If the participant wants to know more about it, they can contact the promoter's Data Protection Officer [protecciódedades@imim.es]

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COLLECTION AND USE OF BIOLOGICAL SAMPLES

The samples obtained during the development of the study will be analyzed in the laboratory of the Hospital del Mar-IMIM. During this process, the person responsible for the samples will be the promoter of the study. It is planned to create a collection with surplus samples for future research related to the research line of the study. This collection will be conveniently declared and registered in the National Registry of Biological Sample Collections of the Carlos III Health Institute. These samples will only be used for projects related to the line of research, favorably reported by a Research Ethics Committee and will not be transferred to third parties. In the event that there is a surplus of sample once the line of research has been completed, they will be transferred to the MARBiobanc Biobank (Biobank of the Parc de Salut Mar, B.0000665; the Director of the same being Dr. Montserrat Torà Barnadas) registered in Spain (Institute de Salud Carlos III) so that it can be preserved and used in future biomedical research projects that comply with the applicable ethical and legal principles. The donation will be made in an encrypted way, to guarantee the protection of your identity. The clinician responsible for the research will deliver to the Biobank the associated clinical data, or that will be associated in the future, when they are relevant for biomedical research purposes, and the sample, in accordance with their will, for storage in the Biobank facilities. In your hospital, the data that could be related to the samples to be kept will be recorded, using a coding procedure to guarantee the protection of your identity. Only the clinical manager of this donation will be able to relate this data to you. At all times, the ethical and legal requirements set forth in RD 1716/2011 will be complied with. At any time you may revoke the consent granted to the Biobank for its use, being able to request its destruction. However, the effects of the revocation will not extend to the data resulting from the investigations that have been carried out prior to it. For more information about your rights of access, rectification, cancellation and opposition you can exercise them, if so. wishes, with ..... the results of futures

Studies may be communicated at scientific meetings or scientific publications. Your identity will be kept strictly confidential.

CONTACT IN CASE OF DOUBTS

Dr/Dra: Robert Güerri-Fernández (rguerri@psmar.cat) or Silvia Gómez-Zorrilla Martín.

Infectious Diseases Service. hospital of the sea

Contact telephone number *:* 932483468

INFORMED CONSENT FORM

Study Title: Immune Boost with Zinc Supplements to Reduce Inflammation, Viral Load, and Mortality in COVID-19 Infection.

Version and date of the Informed Consent: version 1.0, February 12 , 2021.

I……

(Name and surname of the participant)

- ✓ I have read and understand the information sheet provided to me .delivered.
- ✓ I have been able to ask questions about the study and they have been answered.
- ✓ I have received enough information about the study.
- ✓ I understand that my participation is voluntary.
- ✓ I understand that I can withdraw from the study: 1º When want.
  2º Without giving explanations.
  3º Without this affecting my medical attention.

I freely give my agreement to participate in this study and my consent for the access and use of my data under the conditions detailed in the information sheet. I will receive a signed and dated copy of this informed consent.

Fullfill by patient ONLY
Date:_____/_____/_____ **Signature:**

Fullfill by investigator
Date:_____/_____/_____ **Signature:** **Name:** _____

I consent to the storage and use of biological samples and associated data for future research under the conditions explained in this information sheet.

yes ☐ no ☐

Name and surname of the participant: _____

Date: __/__/_____

Signature:

Name and surname of the researcher :_____

Date: __/__/_____

Signature:

CONSENT FORM OF THE LEGAL REPRESENTATIVE, FAMILY MEMBER, OR FACTUALLY RELATED PERSON

(when the IQ is obtained in people with modified ability to give their IQ)

Study Title: Immune Boost with Zinc Supplements to Reduce Inflammation, Viral Load, and Mortality in COVID-19 Infection.

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I…….. …….

(name and surname of the legal representative, family member or person related in fact) In quality of representative

of:……

(patient's first and last name)

- ✓ I have read and understand the information sheet provided to me .delivered.
- ✓ I have been able to ask questions about the study and they have been answered.
- ✓ I have received enough information about the study.
- ✓ I understand that my participation is voluntary.
- ✓ I understand that I can withdraw from the study: 1º When want.
  2º Without giving explanations.
  3º Without this affecting my medical attention.

The subject has received in my presence all relevant information adapted to his level of understanding and agrees to participate.

I freely agree to the subject 's participation in the study. I authorize the use and transmission of your health data under the conditions detailed in the information sheet . I will receive a signed and dated copy of this consent informed.

Fullfill by familiar or authorised person
Fecha:_____/_____/_____ **Firma:**

Fulfill by investigator
Fecha:_____/_____/_____ **Firma:** **Nombre y apellidos:**_____

I consent to the storage and use of biological samples and associated data for future research under the conditions explained in this information sheet.

yes ☐ no ☐

Name and surname of the **competitor:**_____

Date:__/____/_____

Signature:

Name and surname of the **researcher** :_____

Date:__/____/_____

Signature:

Name and surname of the **legal representative, family member or person linked in fact** (when the IQ is obtained in people with modified ability to give their IQ)

Date:__/____/_____

Signature: