Title of the research:
Anticoagulation in Patients with Severe COVID-19: a Multicenter, Parallel-group, Open-label, Randomized Controlled Trial
(ANTICOVID)

This research is promoted by *Assistance Publique - Hôpitaux de Paris*
Represented by the Director of
***Direction de la Recherche Clinique et de l'Innovation* (DRCI)**
1 avenue Claude Vellefaux
75010 Paris

PARTICIPATION INVITATION

Dear Madam, dear Sir

Dr./Pr. (delete as appropriate)..... (First name, Surname), working at ……. Hospital, invites you to participate in a research study conducted to examine your disease.
We highly encourage you to read this document carefully before making any decision. Do not hesitate to ask for further information.
If you agree to participate in this research, you will be asked to sign a written consent.

1) What is the objective of this research?

You are admitted to hospital to be treated for COVID-19. The study you are asked to take part in assesses the different approaches used to prevent blood clotting (anticoagulation) in patients with COVID-19, either with high dose (therapeutic), low dose (standard prophylactic) or intermediate dose (intermediate prophylactic) anticoagulation. The three options are currently employed in the management of COVID-19.
To perform this research study, we intend to include 353 of the COVID-19 patients who are admitted to French hospitals.

2) What does the research consist in?

COVID-19 may trigger excessive coagulation leading to the development of blood clots in the lung vessels (pulmonary thrombosis). Some middle and big-size clots can be seen via an imaging technique called chest Computed Tomography with Pulmonary Angiogram (CTPA), but not the small clots.
If you agree to participate in this study, we will do CTPA since it is a standard investigation tool to look for pulmonary thrombosis in COVID-19 patients.
If your CTPA is positive, you will receive anticoagulant treatment at a therapeutic dose for three months, as recommended.
If your CTPA is negative, you will receive anticoagulant treatment, either at standard prophylactic (low) dose, intermediate prophylactic (intermediate) dose, or therapeutic (high) dose. The anticoagulant dose will be randomly selected (this random selection is called randomization). Except in particular conditions, the anticoagulant is tinzaparin, of which you will take one subcutaneous injection a day for 14 days.
In all cases, you will also receive the recommended treatment for COVID-19 throughout your hospitalization.

3) What is the work schedule of the research?

The research is expected to take 6 months and your participation 90 days (3 months). After signing your consent form at the first visit, your participation in the study will start. If you did not undergo CTPA within the three days prior to inclusion, new CTPA would be performed within 24 hours of your inclusion in this study. If your CTPA is negative for thrombosis, the dose of anticoagulant therapy will be randomized within 24 hours of CTPA. This randomization is performed at the first day of the study (D1).

You will receive the randomized strategy for 14 days, from D1 to D14. Your monitoring data (routine clinical examinations and blood tests) will be daily collected during your hospitalization. For a better assessment of your health status, your follow-up in this study will take three months. The evolution of your condition (vital status, oxygen support, and other complications) will be evaluated at D28 (or at discharge if it occurs before D28). You will receive a telephone call at month 3 of follow up to assess your quality of life. The follow-up will be identical for all patients included in the study, whether randomized or not.

4) What are the benefits of your participation?

By participating in this research, you will benefit from regular medical follow-up at no additional cost. Intermediate prophylactic and therapeutic anticoagulation strategies could decrease the duration of COVID-19 as well as its mortality. In addition, your participation will help us deepen our knowledge about COVID-19 treatment.

5) What are the anticipated risks and constraints added by the research?

Anticoagulation can induce bleeding (major bleeding is exceptional). The study approaches are already part of the routine medical treatment of COVID-19 patients. Therefore, there is no risk specifically related to this research. Close monitoring, as is the standard protocol in patients hospitalized for COVID-19, will be performed during hospitalization.
If you agree to participate, you should respect the following point: not to participate in another research project without your doctor's approval, in order to protect yourself from any health problems that could result, for example, from possible incompatibilities between the studied drugs or from other exposures.

6) What are the potential medical alternatives?

If you choose not to participate in this research, you will receive appropriate healthcare according to your condition, in compliance with standard clinical practice.

7) What kind of medical care to have after participation?

The follow-up is not specific for this study. You will continue to receive the care adapted to your health condition whether it concerns the usual management in case of premature interruption of the research or the care to receive at the end of your participation.
Your doctor may decide at any time to stop your participation and should explain the reasons to you.

8) If you participate, how will your collected data be used in the research?

Within the framework of the research you are invited to participate in, the treatment of your personal data will be carried out by AP-HP, the research promoter in charge of data management, to analyze the results.

This data processing is necessary to carry out research of public health interest, which comes in alignment with the missions of AP-HP as a public university hospital.

For this purpose, your medical and lifestyle data will be transmitted to the Promoter or to persons or partners working on its behalf, in France or abroad. Such data will be identified by a registration number. As well, such data could be transmitted to French or foreign health authorities, under conditions that guarantee their confidentiality.

It is also possible that your medical data, which could be documented in reports by competent authorities interested in the strategies evaluated in this research, be transmitted to an industrial company in order to allow a greater number of patients to benefit from the results of this research. This transmission will be done under conditions that guarantee confidentiality.

Your data could be used in further research work or complementary analysis in collaboration with private or public partners, in France or abroad, under conditions that guarantee their confidentiality and the same level of protection as stated by the European legislation.
You can object to any further analysis of your data at any time by informing the doctor who is following you in this research.

Your data will only be kept for as long as is strictly necessary and warranted by the research purpose. It will be stored in the information systems of the data manager for two years after the last publication of the research results. Your data will then be archived in fulfilment with the regulations in force.

The database used in this research is established in compliance with the French (modified "*Informatique et Libertés*" law) and European (*Règlement Général sur la Protection des Données* - RGPD) laws. You have the right to access, modify, restrict, and object to the processing of data which are covered by professional secrecy and used in the framework of this research.

If you decide to stop your participation, the data collected prior to this decision will be used in accordance with the regulations and exclusively for the purposes of this research. Deleting them would compromise the validity of the research results. However, from that date on your data will not be further used in this research or in other works.

If you have a problem concerning your rights, you can contact the AP-HP's data protection officer at the following address: protection.donnees.dsi@aphp.fr, who will be able to explain to you the possible channels available for you at the CNIL. You can also use your right to complain directly to the CNIL (for further information on this subject, visit www.cnil.fr).

9) How is this research supervised?

AP-HP has taken all the measures to carry out this research in compliance with the Public Health Regulations applicable to research involving human volunteers.

AP-HP has taken out an insurance policy (number …….) that guarantees its civil liability and that of all those involved with HDI-GERLING company through its insurance broker BIOMEDICINSURE whose address is *Parc d'Innovation, Bretagne Sud C.P.142 56038 Vannes Cedex*.

AP-HP obtained approval from the ethics committee [indicate the name of the CPP] on [indicate the date of the meeting in dd/mm/yyyy format].

10) What are your rights?

Your participation in this research is free and voluntary. Your decision will not compromise the quality of care and treatment you are expected to receive.

Throughout the study period and at any given time, you can ask your investigating doctor for further information about your health as well as explanations of the research process.

You may withdraw from the research at any time without explanation, without any consequences for your treatment or the quality of care you receive, and without any consequences for your relationship with your doctor. After this withdrawal, you may be followed by the same medical team. In this case, the data collected until the withdrawal will be used for the analysis of the research results.

Your medical file will remain confidential and can only be consulted under the responsibility of the doctor in charge of your treatment as well as by the health authorities and by persons who are authorised by AP-HP for research and are subjected to professional confidentiality.

At the end of the study and its data analysis, you can have access to the overall results by asking the doctor who is treating you in the study.

You can also access all your medical data directly or through a doctor of your choice in fulfillment with Article L 1111-7 of the Public Health Regulations.

If you agree to participate in the research after you have read all this information, discussed it with your doctor and had time to think about it, you will be asked to sign and date the informed consent form at the end of this document.

ASSISTANCE PUBLIQUE HÔPITAUX DE PARIS

CONSENT FORM

I, the undersigned, Ms., Mr. [delete as appropriate] (First name, Surname) ..... voluntarily agree to participate in the study entitled

"Anticoagulation in Patients with Severe COVID-19: a Multicenter, Parallel-group, Open-label, Randomized Controlled Trial"

promoted by *Assistance Publique - Hôpitaux de Paris* and I was informed about by Dr./Pr. (name, surname, telephone)....., investigator of this research.

- I have read the participation invitation version 1.0 of 18/12/2020 (3 pages), which explains the purpose of this trial, how it will be conducted, and what my participation will consist of;
- I will keep a copy of the participation invitation and the consent form:
- I have received appropriate answers to all my questions;
- I have had sufficient time to make my decision;
- I have understood that my participation is free and that I can stop my participation at any time, without any liability and without prejudices to the quality of care I will receive;
- I have been informed that the data collected in the research may be used for other studies, and that I can object to that at any time;
- I am aware that my participation can also be interrupted whenever necessary by the doctor who should then explain the reasons;
- I have been informed that my participation in this research will last three months during which I cannot consider participation in another research without informing the investigating doctor in charge of my case in this trial,
- My consent in no way releases the doctor who is following me in the research nor AP-HP from all their responsibilities, and I retain all rights guaranteed to me by the law.

Signature of the participating person		**Signature of the doctor**	
First name, Surname:		Fist name, Surname:	
Date:	Signature:	Date:	Signature:

This document must be produced in three copies: one copy must be kept by the investigator for 15 years, the second given to the consenting person, and the third sent to AP-HP in a sealed envelope at the end of the study.