

Northwell Health

Consent for Participation in a Research Study

Study Title: Systemic Anticoagulation with Full Dose Low Molecular Weight Heparin (LMWH) Vs. Prophylactic or Intermediate Dose LMWH In High Risk COVID-19 Patients (HEP-COVID Trial)

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About this research

You are being asked to participate in a research study.

This consent form will give you information about the study to help you decide whether you want to participate. Please read this form, and ask any questions you have, before agreeing to be in the study.

Important Information

This information gives you an overview of the research. More information about these topics may be found in the pages that follow.

Why am I being asked to provide my consent?	This is a research study, which is different than personal medical care. Scientists do research to answer important questions which might help change or improve the way we do things in the future.
Do I have to join this research study?	No. Taking part in this research study is voluntary. You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled.
Why is this research study being done?	The purpose of this research study is to find out whether Full Dose Heparin (LMWH) or Prophylactic (preventative)/Intermediate Dose Heparin (LMWH) is a safe and effective treatment in COVID-19 Hospitalized Adults.
What will happen to me during the study?	You will be given Full Dose Heparin (LMWH) or Prophylactic(preventive)/Intermediate Dose Heparin (LMWH) to treat your illness while you are hospitalized. When you leave the hospital, we will follow-up with you within 30 days. Heparin (LMWH) is commonly used to treat or prevent blood clots but we do not know if it works against COVID-19.
How long will I participate?	You will be in this study for a total of 30 days. You will receive medication during your hospitalization for COVID-19. Whether you are in the hospital or at home, we will follow-up with you in 30 days.
Will taking part expose me to risks?	Taking any medication exposes you to a risk of side effects. It is possible that Heparin (LMWH) may cause bleeding including bleeding gums, nosebleeds, prolonged bleeding from cuts, anemia, diarrhea, nausea,

	fever, edema, leg swelling, difficulty breathing, confusion and injection site pain. In some cases there have been reports of spinal/epidural hematomas (accumulation of blood around the spinal cord) in patients receiving local anesthesia around the spine or spinal cord or undergoing spinal puncture. There is also an unlikely risk of serious allergic reaction while taking Heparin (LMWH). With any research study that collects personal information, there is a small risk of loss of confidentiality.
Are there any benefits to participation?	If the medication being studied is effective against COVID-19, participation in this research study may benefit you directly. Information learned in this study will help us to better treat future patients.
What are my alternatives to participation?	If you do not participate in this study, you will not receive the medications being studied. You will receive the current standard of care for COVID-19.

Please review the rest of this document for details about these topics and additional things you should know before making a decision about whether to participate in this research.

As the participant's legally authorized representative or next of kin, you are being asked to give consent for the participant to be in a research study. You are being asked to do this because the participant is not able to give consent. When making this decision you should take into account the wishes of the participant. If you agree to allow the participant to take part in this research, the participant will also be asked to give consent if the ability to make healthcare decisions is regained.

Introduction

You are being asked to join a research study. The purpose of a research study is to answer specific questions, sometimes about the safety of a drug or device and how well it works. Being in a research study is different from being a patient. When you are a patient, you and your doctor have freedom in making decisions about your healthcare. When you are in a research study, the researcher will follow the rules of the research study as closely as possible, while monitoring your health.

You do not have to be in this study to receive medical care. You should ask questions before you decide if you want to participate. You can also ask questions at any time during the study.

Why is this research study being done?

The purpose of this research is to compare two different dosing mechanisms of Heparin (LMWH), a medication commonly used to treat and prevent blood clots, to find out if they are effective against COVID-19.

Heparin (LMWH, brand name: Enoxaparin) is drug that has already been approved by the Food and Drug Administration (FDA) for preventing blood clots in patients. However, the higher-than usual treatment dose (full dose) has not been studied in preventing blood clots, in terms of safety and effectiveness, specifically in COVID patients. In this study, the researchers are testing

whether the treatment dose (full dose) of Heparin (LMWH) or the usual low (preventative) dose is more effective in preventing blood clots in hospitalized COVID patients.

You are being asked to participate in this study because you have been diagnosed with COVID-19 and are being admitted to the hospital for treatment.

How many people will take part in this study?

This research study hopes to enroll a total of 308 study participants and approximately 200 study participants will be recruited across multiple sites within the Northwell Health System and the remaining 108 subjects will be recruited at external sites.

How long will you be in this study?

If you choose to take part in this study, the study procedures will last for the entire time you are admitted to the hospital, which will be a minimum of 72 hours, and you will be followed for 30 days after study entry. If you leave the hospital prior to the 30 day time point, you will have a follow-up via telephone or in-person.

What will happen in this research study?

In this study you will be randomized to one of two different treatment groups after giving informed consent and within 72 hours of initial (index) hospitalization. This means that you will be assigned to a group by chance (like flipping a coin). You will have an equal chance of being in either group. Both study groups will receive treatment. The study is done this way because knowing which treatment group you are assigned to can change the results of the study. We will not tell you which group you are in to prevent study bias. However at any point we can quickly find out which group you are in if we ever need to know for your safety. The different treatment groups are as following:

- 1) Patients will receive the standard of care plus open label therapeutic dose Heparin (LMWH)
- 2) Patients will receive the standard of care plus Prophylactic (preventive) or Intermediate dose Heparin (LMWH)

No other anticoagulation medicines except Heparin (LMWH) will be permitted for the duration of your hospital stay. You will receive study medication throughout your hospitalization until the time of hospital discharge.

In addition to the standard current treatment for COVID-19, you will undergo a imaging scan of your lower body (legs, thighs, etc.) at Hospital Day 10+4 or sooner at the time of hospital discharge using standardized screening methods. After hospital discharge you will continue a low dose blood thinner (either prophylactic dose LMWH or an oral agent rivaroxaban) for up to 39 days as per standard of care.

You will stay in the hospital for as long as is needed to treat you. All other procedures will be done as part of the current standard of care for COVID-19 and may include having your blood drawn.. We will collect the results of those and any other tests done and record them for this study.

Birth Control

The drugs in this study may affect a baby, before or after the baby is born. As a result, women should not be in this study if they are:

- pregnant,
- breast-feeding, or
- trying to become pregnant.

If you are a woman of childbearing age, you should use birth control for the entire time you are in the study. Your doctor will discuss these with you.

What are the risks of the research study? What could go wrong?

Heparin (LMWH) is a drug commonly used to treat and prevent blood clots. It is possible that Heparin (LMWH) may cause bleeding including bleeding gums, nosebleeds, prolonged bleeding from cuts, anemia, diarrhea, nausea, fever, edema, leg swelling, difficulty breathing, confusion and injection site pain. In some cases there have been reports of spinal/epidural hematomas (accumulation of blood around the spinal cord) in patients receiving anesthesia around the spine or spinal cord, or undergoing spinal puncture. Heparin (LMWH) has been reported to cause warmth or bluish-colored skin in some patients. Lastly, there is an unlikely risk of serious allergic reaction while taking Heparin (LMWH).

Thus, as with any drug there might be side effects that are unknown at this time. You will be closely watched for side effects. You should report any unusual events to the study staff. Because you are being randomized to a study group, your group may receive less effective treatment or have more side effects than the other group. We do not know if one group is more effective than the other.

With any research study that collects personal information, there is a small risk of loss of confidentiality.

Blood-Draw

There are no major risks of having blood drawn. It can be uncomfortable and can sometimes cause a bruise. In rare cases, it can cause fainting. Only trained staff will draw your blood.

What are the benefits of this research study?

If the medication being studied is effective against COVID-19, participation in this research study may benefit you directly. It is possible that your study group might receive more effective treatment and/or have fewer side effects than the other treatment groups. Information learned in this study may help us to treat future patients.

If you do not want to take part in this research study, what are your other choices?

If you do not join this study, you have other choices for treatment. Talk to your doctor about your choices. Your other choices may include:

- Another research treatment
- Standard treatment

- No treatment
- Comfort care
- Heparin (LMWH) without participating in this study.

Your doctor can also tell you the important risks and benefits associated with the alternative treatment.

Are there any costs for being in this research study?

You will not have any added costs from being in this study. The study medication will be provided to you at no cost. All other costs are part of the standard of care and will be billed to you and your insurance company in the usual way, as part of your standard care.

Will you receive any payments for participating in this research study?

You will not be compensated for participation in this research study.

What happens if you are injured while participating in this study?

If you are hurt from being in the study, you will receive medical care and treatment as needed from Northwell Health. However, you will be responsible for the costs of such medical treatment, directly or through your medical insurance or other forms of medical coverage. No money will be given to you.

What are your rights as a research participant?

Your participation in this project is voluntary. The quality of your medical care will be the same, whether you join, refuse to join, or decide to leave the study.

If you do not join the study you will not be penalized or lose benefits to which you are entitled. If you join the study you may withdraw at any time without prejudice to your future care at Northwell Health. Follow-up examinations may be needed to assure your well-being.

Could you be taken off the study before it is over?

It is also possible that your participation in this study may end without your consent. This decision may be made by a researcher, study sponsor or the Institutional Review Board (IRB- the committee that oversees research at this institution).

Reasons for withdrawal may include:

- failure to follow instructions,
- failure to show up for study visits,
- it is not in your best interest to continue on this study, or
- the study is stopped.

If you withdraw from this study or if you are withdrawn from the study, any data (or samples) already collected will continue to be used. However, no new data will be collected.

What happens if new information is learned?

You will be told of any new findings that may change your decision to continue to participate. Your consent to continue to take part in this study may be obtained again.

What information will be collected and used for this study?

If you agree to be in this study, we will collect health information that identifies you. We may collect the results of lab tests and medical examinations done while you are in the hospital. We will also collect one extra tube of blood (e.g. approx. 1-2 tablespoons) during routine blood draws while you are hospitalized. These samples will be stored for this research study, but will not identify you. We may also collect information from your medical record. We will only collect information that is needed for the research. This information has been described in this consent form. If you sign this consent form, you are giving us permission to collect, use and share your health information. This permission is called authorization. If you do not want to provide authorization, then you cannot participate in this research study.

Who else will see your information?

Study records that identify you will be kept private. You will not be identified in study records or publications disclosed outside Northwell Health, except as detailed below. Investigators will share information collected from this research study with:

- other researchers,
- accrediting agencies,
- data safety monitoring board,
- clinical staff not involved in the study who may be involved in participant's treatment,
- health insurers or payers

The following reviewers may access your study and medical records to make sure that this study is being done properly:

- Representatives from Federal and state government oversight agencies, such as the Food and Drug Administration (FDA)
- Representatives from Northwell Health's Human Research Protection Program (a group of people that oversee research at this institution)

We will do our best to protect the privacy of your records but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by the federal law.

In the future, we may publish results of this study in scientific journals and may present it at scientific meetings. If we do we will not identify you.

If the researchers learn about potential serious harm to you or someone else or other public health concerns, it will be shared with the appropriate authorities.

Will you be able to access your records?

If your research records are used for decisions related to your clinical care, then you have the right to review this information and request changes. This is limited to information about your

treatment, and does not include information related to procedures or tests that are for research purposes only. You may access this information only after the study analysis is complete. You have the right to know who has and who will see your records. To request this information, please call the Human Research Protection Program at 516-465-1910.

How long will your health information be kept?

There is no limit on the length of time we will keep your information for this research because it may be analyzed for many years. We will keep it as long as it is useful, unless you decide you no longer want to take part or we close the study. You are allowing access to this information indefinitely.

Can you change your mind?

If you change your mind about being in the study, you may withdraw at any time. If you want us to stop collecting your health information, you need to send a letter to the researcher at the following address:

Dr. Alex C. Spyropoulos, MD, FACP, FCCP, FRCPC
600 Community Drive, Suite 403
Manhasset, NY 11030

Your letter needs to say that you have changed your mind and do not want the researcher to collect and share your health information. You may also need to leave the research study if we cannot collect any more health information. We may still use the information we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

Will information about this study be available to the public?

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this website at any time.

Will my information be used for research in the future?

Information or specimens collected from you for this research may be used for future research studies or shared with other researchers for future research. If this happens, information which could identify you will be removed before any information or specimens are shared. Since identifying information will be removed, there will not be an additional consent for future research. By consenting to participate in this study you are agreeing to allow your de-identified specimens and/or data to be used by future researchers without additional consent.

Does the investigator of this study receive money if you take part?

The investigators on this study do not receive money for your participation in this study.

Who can answer your questions about this study?

If you have any questions about the study, you may call Dr. Alex C. Spyropoulos at (212) 434-6776. If you have questions about side effects or injury caused by research you should call Dr. Alex C. Spyropoulos at (212) 434-6776. If you need emergency care, dial 911 or go to the

nearest Emergency Room. If you have questions about your rights as a research participant, concerns about being in the study, or would like to offer input, you may contact the Office of the Institutional Review Board (the committee that oversees research at this institution) at (516) 465-1910.

A signed copy of this consent form will be given to you.

[Signature Page Follows]

Summation/Signature

You have read the above description of the research study. You have been told of the risks and benefits involved and all your questions have been answered to your satisfaction. A member of the research team will answer any future questions you may have. You voluntarily agree to join this study and know that you can withdraw from the study at any time without penalty. By signing this form, you have not given up any of your legal rights.

Signature of Participant/Healthcare Agent/Guardian/Next of Kin

Date

Printed Name of Participant /Healthcare Agent/Guardian/Next of Kin**Impartial Witness Signature Section (if applicable)**

Signature of Impartial Witness

Date

Printed Name of Impartial Witness**Investigator's Statement**

In addition to advising the above participant of other forms of treatment and therapy which are appropriate, I have offered an opportunity for further explanation of the risks and discomforts which are, or may be associated with this study and to answer any further questions relating to it.

Investigator's signature

Date

Investigator's printed name