

Title: A Phase II Study Evaluating Fostamatinib for Hospitalized Adults with COVID-19

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PRINCIPAL INVESTIGATOR: Jeffrey R. Strich, MD

STUDY TITLE: A Phase II Study Evaluating Fostamatinib for Hospitalized Adults with COVID-19

STUDY SITE: NIH Clinical Center

Cohort: *Affected patient*

Consent Version: 02/05/2021

WHO DO YOU CONTACT ABOUT THIS STUDY?

Jeffrey Strich, MD: strichj@niaid.nih.gov; 301-496-9320

Jennifer Kyte, RN, DNP, ACNS-BC: jennifer.kyte@nih.gov; 301-827-0367

KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

The purpose of this research study is to find out whether a drug called fostamatinib is safe for patients seriously ill with COVID-19, and if this drug can improve the patients' health.

Fostamatinib has not been approved to treat COVID-19. However, the use of fostamatinib is approved to treat immune thrombocytopenia (bleeding disorder). We are testing it in this research study to see if fostamatinib can improve patients' health when they are seriously sick with COVID-19.

While in a hospital, you will be treated for COVID-19 in accordance with the current medical standard of care. Your doctors will decide what the best treatment options for you are. Joining this study will not affect your standard COVID-19 treatment.

If you decide to take part in this study, in addition to your standard COVID-19 treatment you will be taking either fostamatinib pills or placebo ("dummy" pills). Also, as part of this study, you will undergo frequent blood tests to check your health and how your body responds to the research treatment. Your involvement is expected to last for about two months.

Known side effects of fostamatinib include diarrhea, high blood pressure, nausea, respiratory infection, dizziness, increased liver enzymes, rash, abdominal pain, fatigue, chest pain, and low blood counts.

PATIENT IDENTIFICATION

Consent to Participate in a Clinical Research Study

NIH-2977 (4-17)

File in Section 4: Protocol Consent (1)

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IRB NUMBER: 000110

IRB APPROVAL DATE: 02/16/2021

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being asked to participate in this research study is not able to give consent for themselves, you, as the Legally Authorized Representative, will be their decision-maker and you are being asked to give permission for this person to be in this study. For the remainder of this document, the term “you” refers to you as the decision-maker and/or the individual being asked to participate in this research.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to find out whether a drug called fostamatinib is safe and if it can improve patients’ health when they are seriously ill with COVID-19.

COVID-19 is a new disease caused by a virus that was just identified in 2019. Some people who become sick with COVID-19 become seriously ill and must be hospitalized. There are some medicines that may assist patient’s recovery. There are no medicines that cure the disease. Some hospitalized patients die even after all treatment options have been given.

Early data suggest that a drug called fostamatinib may help patients with COVID-19. This study will test fostamatinib in adults that are hospitalized with COVID-19.

We want to compare the effect of giving fostamatinib pills with placebo pills. The placebo “dummy” pill looks like the real drug but does not have the drug in it. Using a placebo is common in research studies.

We are asking you to join this research study because you have been diagnosed with COVID-19 and are currently hospitalized.

Fostamatinib is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) to treat COVID-19. However, the use of fostamatinib is approved to treat immune thrombocytopenia (bleeding disorder). We are testing it in this research study to see if fostamatinib can improve patients’ health when they are seriously sick with COVID-19.



WHAT WILL HAPPEN DURING THE STUDY?

While in a hospital, you will be treated for COVID-19 in accordance with the current medical standard of care. Your doctors will decide what are the best treatment options for you. Joining this study will not affect your standard COVID-19 treatment.

Before you begin the study

If you decide to take part in this study, you will be asked to do some tests to make sure it is safe for you to join.

- **Physical examination**, including weight and vital signs
- **Blood test** to evaluate your liver, kidney and immune system
- **COVID-19 test** (if not taken already within 7 days) will be performed as an oropharyngeal swab (swab of the back of your throat) or a nasopharyngeal swab (swab of the back of your nose)
- **Pregnancy test** (if you are a woman who can have children)
- **Chest X-Ray** will be done to check the condition of your lungs

During the study

Study drug:

If you join the study, you will be randomly put into one of two groups. This is decided by chance, similar to flipping a coin. Out of every 2 people on this study, 1 will get fostamatinib, and 1 will get placebo. You will have an equal chance of being in either of the study groups. You and the study staff will not know what group you are in. When the study is over, we will learn if fostamatinib is safe and more successful in treating people with COVID-19 than standard of care alone.

After all participants have completed the study, we will contact you to tell you whether you got fostamatinib or the placebo.

You will get fostamatinib pills or placebo pills for 14 days.

- If you get fostamatinib, the dose will be 150 mg twice daily. The placebo pills will look like the study drug but do not have the drug in it. If you are able to swallow, the pills will be taken by mouth with water. If you are unable to swallow or on mechanical ventilation, the pills will be crushed, mixed with water and given to you through a orogastric (OG) or nasogastric (NG) tube that carries medicine to the stomach through the mouth or nose. Your doctor or nurse will insert a thin plastic tube through your nostril, or your mouth down your esophagus, and into your stomach. Once this tube is in place, they can use it to give you medicine.
- If you recover and are discharged prior to day 14, you will be given the pills to take home with you, and to continue taking them up until day 14.
- If at any time your doctor determines that it is no longer safe for you to take the study drug, the drug will be discontinued. If this happens, you will still need to complete blood tests and follow-up visits described below.



Blood Tests: While you are in a hospital, we will be taking samples of your blood for health tests on approximately days 1, 3, 5, 8, 11, 15, 22, 29, and 60, unless you are discharged earlier than that. Blood tests may be done more frequently, as often as once daily if initial blood work shows some abnormalities.

Additionally, on those days we will be taking about 3 tablespoons of your blood for research purposes, to check how your body responds to the treatment. Once you are discharged from the hospital, we will draw your blood during follow-up visits as described below.

Follow Up Visits: After your discharge, you will be asked to return to Clinical Center for a safety follow up visits on approximately days 5, 8, 11, 15, 22, 29, and 60. At these visits you will get blood draws for health checks and research tests, your vital signs will be taken, and you will be asked questions about your health. If you are unable to visit the Clinical Center, the doctor will speak to you on the phone, or will arrange a telehealth visit, or outside lab visit. If you are still hospitalized on those days, these checks will be done by the study group at the hospital.

COVID-19 swab test will be done on approximately days 1, 3, 5, 8, 11, 15, 22, 29, and 60 during your participation in the study to study how the virus is cleared by the body.

What you should avoid during your participation in this study

- While participating in this study you should refrain from drinking alcohol.
- If you are a woman who can have children, once discharged, you should avoid pregnancy through abstinence or use of at least one contraceptive until 30 days after last day of study drug.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last for about 60 days. It will include your time in the hospital and follow up visits to the Clinical Center. Visits usually take about 1 hour, but may be longer.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 10 people participate in this study at the NIH.

Up to 80 people might also participate at other study sites.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

Blood draws

We will insert a new, clean needle into a vein in your arm to take blood. You may feel a pinch when the needle goes through your skin. A bruise may appear where it was put in. You may also have swelling, and the area may be sore. These things are common and should go away in a couple of days. If you already have a central line in place, we will draw the blood from that line.

Orogastric (OG) or nasogastric (NG) tube insertion

If your NG tube isn't inserted properly, it can potentially injure the tissue inside your nose, sinuses, throat, esophagus, or stomach. This is why placement of the NG tube is checked and confirmed to be in the correct location before any other action is performed.

Chest X-Ray

If you haven't had a chest X-ray, while hospitalized, we will ask for one. Chest X-ray is a quick and painless procedure that involves standing or lying on your back in front of X-ray machine. There are no discomforts associated with X-ray scan.

COVID swab test

The test has few risks. You may gag a little during the test. You may also feel slightly uncomfortable, but you shouldn't feel any pain. You may have a minor nosebleed afterwards.

Placebo Pills

There are no risks of taking placebo pills, but you will not know if you are taking placebo pills or the study drug.

Potential Risks of Fostamatinib

Based on the studies conducted to date with fostamatinib, the following side effects are considered possibly related to the use of fostamatinib:

- Very Common; may affect more than 1 in 10 people
 - Diarrhea (includes frequent bowel movement)
 - High or increased blood pressures (hypertension)
 - Shortness of breath, tightening in the chest, difficulty breathing
 - Nausea
 - Dizziness
 - High levels of certain liver blood tests (increased liver enzymes, increased alanine aminotransferase or increased aspartate aminotransferase)
- Common; may affect up to 1 in 10 people
 - Red and/or bumpy rash
 - Upper and lower respiratory tract infection
 - Chest pain not caused by heart disease
 - Fatigue
 - Decreased number of white blood cells that fight infection (neutropenia)
 - Abdominal pain (includes upper abdominal pain)
 - Abnormal taste
 - An inflammation of lining in the tubes carrying air to your lungs (bronchitis)

These side effects usually go away when the drug is stopped.

If you are experiencing significant diarrhea, or stomach or abdominal pain, please tell your study doctor. Your study doctor may provide you with medications to ease these symptoms and allow you to continue to participate in this study.

There is a possibility of allergic reaction to fostamatinib, like rash, hives, itching with or without fever, tightness in the chest or throat, wheezing, trouble breathing or talking, unusual hoarseness,

or swelling of the lips, mouth, face, throat, or tongue. Contact the study doctor immediately, if you should experience any of these symptoms.

What are the risks related to pregnancy?

If you are able to become pregnant, we will ask you to have a pregnancy test before starting this study. You must use effective birth control methods and try not to become pregnant while participating in this study. If you become pregnant, there may be unknown risks to the fetus or unborn child, or risks that we did not anticipate. There may be long-term effects of the treatment being studied that could increase the risk of harm to a fetus. You must tell the study doctor if your birth control method fails while you are in the study. If you think or know you have become pregnant while participating in this research study, please contact the study team as soon as possible. If you plan to become pregnant in the future, please discuss with the study team how long you need to wait before becoming pregnant after completing the study.

If you are a sexually active person with a partner able to become pregnant, it is important that your partner not become pregnant during your participation in this study. There may be unknown risks to a fetus or risks we did not anticipate. You and your partner must agree to use birth control if you want to take part in this study. If you think your partner has become pregnant during your participation in this study, please contact the study team as soon as possible. If you and your partner plan for your partner to become pregnant after your participation in this study, please discuss this with the study team.

What are the risks of radiation from being in the study?

You may not participate in this study if you are pregnant. If you are able to become pregnant, we will perform a pregnancy test before exposing you to radiation. You must tell us if you may have become pregnant within the previous 14 days because the pregnancy test is unreliable during that time.

During your participation in this research study, you will be exposed to radiation from one chest X-ray. This is considered a low exposure. The risk of this exposure is too low to be reliably measured.

Every day, people are exposed to low levels of radiation that come from the sun and the environment around them. This type of radiation is called “background radiation”. No one knows for sure whether exposure to these low amounts of radiation is harmful to your body. The radiation you will get by participating in this study is less than the average yearly background radiation in the United States.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from this study because what we learn in this study may eventually be used to treat others with COVID-19.



WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether or not to be in this study, we will discuss other options that are available to you. Instead of being in this study, you could decide just to be treated for COVID-19 in accordance with the current medical standard of care.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

We do not plan to provide the results from any tests conducted for research purposes only with you or your doctor. However, the information we learn from looking at these research studies may benefit future patients.

EARLY WITHDRAWAL FROM THE STUDY

If at any time your doctor determines that it is no longer safe for you to take the study drug, the drug will be discontinued. If this happens, you will still need to complete blood tests and follow-up visits described above.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you.

Some of your specimens may be sent to our collaborators from other institutions, who will help us with research testing for this study. The specimens will be sent without any personal identification and could never be traced back to you.

Will your specimens or data be saved for use in other research studies?

We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding COVID 19 or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.



I give permission for my coded specimens and data to be stored and used for future research as described above.

Yes No

Initials Initials

Will your specimens or data be shared for use in other research studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas that are similar to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

Yes No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. Usually, these researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.



How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH possibly indefinitely, or until they are no longer of scientific value.

Risks of storage and sharing of specimens and data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT**Will you receive compensation for participation in the study?**

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will receive compensation for the follow up visits after your hospital discharge:

- \$50 for each blood draw;
- \$20 for your first hour, and \$10 for each subsequent hour spent at NIH Clinical Center during the follow up visit;
- If you are unable to finish the study, you will receive compensation only for the parts you completed.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are \$600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH Clinical Center studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

This study does not offer reimbursement for, or payment of, lodging or meals.

For the follow up visits to the NIH Clinical Center you will be reimbursed for your transportation expenses (car mileage, bus, metro, or taxi). If you prefer, NIH can arrange a taxi to take you to the NIH Clinical Center and back home.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

CONFLICT OF INTEREST (COI)

The NIH reviews NIH staff researchers at least yearly for conflicts of interest. This process is detailed in a COI Guide. You may ask your research team for a copy of the COI Guide or for more information. Members of the research team who do not work for NIH are expected to follow these guidelines or the guidelines of their home institution, but they do not need to report their personal finances to the NIH.

The NIH and the research team for this study are using fostamatinib developed by Rigel Pharmaceuticals through a collaboration between your study team and the company. The company also provides financial support for this study.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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 Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- NIH Intramural Institutional Review Board

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.



NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care will be provided by the NIH, the NIH Clinical Center, or the Federal Government. A Declaration under the Public Readiness and Emergency Preparedness (PREP) Act was issued by the Secretary of the United States Department of Health and Human Services on March 10, 2020. This Declaration limits the legal rights of a subject participating in clinical studies utilizing COVID-19 countermeasures. Because this study is covered by the PREP Act Declaration, covered persons, such as the



manufacturers, study sponsor, researchers, healthcare providers and others have liability immunity (that is, they cannot be sued by you or your family under the laws of the United States). If you believe that you may have been harmed as a result of this research study, certain claims for serious injury or death caused by the countermeasure may be eligible for compensation through the Countermeasures Injury Compensation Program. This is a program set up by the United States Government. Information about this program can be found at <https://www.hrsa.gov/cicp/about/index.html> or by calling 1-855-266-2427.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Jeffrey Strich, stichj@niaid.nih.gov; 301-496-9320.

You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.



