Informed Consent Cover Page for FDAAA consent posting:

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PRINCIPAL INVESTIGATOR: Jamie Hur, DO

STUDY TITLE: A Phase II Study using Fostamatinib to treat Post-Hematopoietic Stem Cell Transplant Immune-mediated Cytopenias

STUDY SITE: NIH Clinical Center

Cohort: *Affected patient*

Consent Version: *02/03/2023*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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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 effective in the treatment of post-transplant cytopenia(s).

Fostamatinib has not been approved to treat post-transplant cytopenia(s). 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 post-transplant cytopenia(s).

If you decide to take part in this study, you will be taking fostamatinib pills for 12 weeks. Also, as part of this study, you will undergo blood tests to check your health and how your body responds to the research treatment. Your involvement is expected to last for about 4 months.

The most frequent known side effects of fostamatinib include diarrhea, high blood pressure, nausea, respiratory infections, dizziness, increased liver enzymes, rash, abdominal pain, fatigue, chest pain, and low blood counts. Please talk to your study doctor or other members of the study team if have any questions regarding risks or alternative treatments.

Just as we do not know what side effects you might have; we cannot know if you may benefit from taking part in this study. If you do not benefit, this study and the results from our research will help others in the future.

You are free to stop participating in the trial at any time. If you decide to stop, the study doctor may ask you to agree to certain tests to make sure it is safe for you to stop.

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 effective in the treatment of post-transplant cytopenia(s), including anemia and thrombocytopenia, that is due to immune-related causes.

Cytopenia is a common complication after hematopoietic cell transplantation. Cytopenia(s) occur when one or more of your blood cell types is lower than it should be. Your blood consists of three main parts. Red blood cells, also called erythrocytes, carry oxygen around your body. If the number of red blood cells is below normal limits, it is called anemia. Platelets are essential for clotting. If the number of platelets is below normal limits, it is called thrombocytopenia. Anemia and thrombocytopenia after hematopoietic stem cell transplantation may be immune-mediated, meaning that the red cells, platelets, and/or their progenitor cells, are being targeted by the body's immune system and destroyed.

Early data suggest that a drug called fostamatinib may help patients with immune-mediated cytopenia(s). This study will test fostamatinib in adults with post-transplant cytopenia(s).

We are asking you to join this research study because you have been diagnosed with post-transplant cytopenia(s).

Fostamatinib is considered investigational, which means that it has not been approved by the U.S. Food and Drug Administration (FDA) to treat post-transplant cytopenia(s). However, the use of

fostamatinib is approved to treat immune thrombocytopenia. We are testing it in this research study to see if fostamatinib can improve patients' health when they are sick with post-transplant cytopenia(s).

WHAT WILL HAPPEN DURING THE STUDY?

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.

- **Confirmation of diagnosis.** In order to confirm your diagnosis we will review your medical history, lab test results, and talk to your transplant physician.
- **Physical examination,** including weight and vital signs. We will review any past
- or current medical conditions, and medicines you are taking.
- **Labs: Blood and urine tests**
    - **Routine blood and urine tests** to find out if you have low blood counts, and to evaluate your liver, kidney and immune system.
    - **Stool test.** Your stool sample will be checked for hidden (occult) blood.
    - **Pregnancy test** (if you are a woman who can have children): If you are able to become pregnant, a pregnancy test will be done on your urine sample.
    - **HIV test:** As part of this study, we will test you for infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. If you are infected with HIV you will not be able to participate in this study. We will tell you what the results mean, how to find care, how to avoid infecting others, how we report HIV infection, and the importance of informing your partners at possible risk because of your HIV infection.

During the study

Study drug:

You will get fostamatinib pills for 12 weeks.

- For the first 4 weeks the dose will be 100 mg twice daily.
- After 4 weeks, we will do your blood tests.
- If your cytopenia has improved, you will continue to take 100 mg twice daily up until the end of week 12.
- If your cytopenia has not improved, you drug dose will be increased to 150 mg twice daily, which you will be taking up until the end of week 12.
- 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: during your participation in the study, we will be taking samples of your blood for health tests every 2 weeks (weeks 2, 4, 6, 8, 12 and 14). Blood tests may be done more frequently, if the blood work shows some abnormalities.

Additionally, on those days we will be taking about 3 tablespoons of your blood for research purposes.

Stool test. We will ask you to provide a stool sample to be checked for occult blood every 2 weeks (weeks 2, 4, 6, 8, 12 and 14).

Pregnancy test (if you are a woman who can have children): If you are able to become pregnant, a pregnancy test will be done on your urine sample every four weeks (weeks 4, 8, and 12).

Medical assessment. Every 2 weeks your vital signs will be taken, and the doctor or the research nurse will talk to you about your health.

End of Study Visit: After you have finished taking fostamatinib, you will be asked to return to the Clinical Center for a safety follow up visit on week 14. At this visit you will get blood drawn for health checks and research tests, your vital signs will be taken, and you will be asked questions about your health. Visits usually take about 1 hour, but may be longer.

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 complete the 14 weeks and do not stop the study treatment earlier, you may have an opportunity to enroll in the extension study to continue taking fostamatinib (which involves a separate consent form).

What you should avoid during your participation in this study

- While participating in this study you should refrain from drinking alcohol.
- While participating in this study, you should not become pregnant or father a baby until 30 days after last day of study drug.
- You should refrain from egg or sperm banking/donation from the start of the study drug 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 14 weeks.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 20 people participate in this study at the NIH.

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.

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 (>= 10%); in 100 people taking fostamatinib, 10 and up to 100 may have:
  - Diarrhea (includes frequent bowel movement)
  - Dizziness
  - Blood pressures high or increased (hypertension)
  - Liver blood test levels high (increased liver enzymes, increased alanine aminotransferase, or increased aspartate aminotransferase)
  - Nausea
  - Respiratory tract infection (upper or lower respiratory tract infection, viral respiratory infection)
- Common (>= 1% to < 10%); in 100 people taking fostamatinib, fewer than 9 may have:
  - Abdominal distension
  - Abdominal pain (includes upper abdominal pain)
  - Abnormal taste
  - Appetite decreased
  - Chest pain not caused by heart disease
  - Chills
  - Constipation
  - Enzyme level related to tissue damage high (increased blood lactate dehydrogenase)
  - Fast heart rate
  - Fatigue
  - Flatulence
  - Hair color changes
  - Inflammation of lining in the tubes carrying air to your lungs (bronchitis)
  - Influenza-like illness
  - Liver blood test levels high (increased blood bilirubin)
  - Memory loss or forgetfulness
  - Muscle pain
  - Rash that is red and/or bumpy
  - Sleeping difficulty
  - Swelling in the lower legs and/or hands (peripheral edema)
  - White blood cells that fight infection decreased (neutropenia, leukopenia)

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

If you are experiencing significant diarrhea, or stomach or abdominal pain, please contact your study doctor. These symptoms can become serious and may lead to dehydration and/or require you to go to the hospital. Your study doctor may instruct you to make changes to your diet or provide you with medications to ease these symptoms and allow you to continue to participate in this study.

You should talk to your study doctor about any side effects that you have while taking part in the study. You should tell the study doctor if you have any problems with your health or the way you feel while taking part in the study, whether or not you think it is related to the study.

In addition to the risks or discomforts listed here, there may be other risks that are currently not known. Also, the risks or discomforts described may occur more often or be more severe than has been seen before.

Allergic Reaction Risks

Sometimes people have allergic reactions to drugs. Some signs that you may be having an allergic reaction are:

- Rash or hives
- Having a hard time breathing
- Wheezing when you breathe
- Sudden change in blood pressure (making you feel dizzy or lightheaded)
- Swelling around the mouth, throat or eyes
- Fast pulse
- Sweating

Some allergic reactions can be serious and life-threatening, and very infrequently may result in death. You should get medical help and contact the study doctor or staff if you have any of these or any other side effects during the study.

The study drug must be taken only by you. It must be kept out of the reach of children and others.

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 try not to become pregnant while participating in this study. You and your partner must avoid pregnancy through abstinence or the use of 2 forms of highly effective birth control until 30 days after last day of study drug if you want to take part 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 avoid pregnancy through abstinence or the use of 2 forms of highly effective birth control until 30 days after last day of study drug 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.

Both male and female patients must not donate eggs or sperm during the course of the study and for until 30 days after last day of study drug..

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, the potential benefit to you might be the improvement of your post-transplant cytopenia(s) and symptoms associated with it.

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 post-transplant cytopenia(s).

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 post-transplant cytopenia(s) 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 you or your doctor with the results from any tests conducted for research purposes only. However, the information we learn from looking at these research studies may benefit future patients.

EARLY WITHDRAWAL FROM THE STUDY

Your doctor may decide to stop your therapy for the following reasons:

- if he/she believes that it is in your best interest
- if your disease worsens
- if you have side effects from the treatment that your doctor thinks are too severe
- if you become pregnant
- if you do not follow the study rules

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 visit described above.

You can stop taking part in the study at any time. However, if you decide to stop taking part in the study, we would like you to talk to the study doctor and your regular doctor first.

If you decide at any time to withdraw your consent to participate in the trial, we will not collect any additional medical information about you. However, according to FDA guidelines, information collected on you up to that point may still be provided to Rigel Pharmaceuticals or designated representatives.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved by the study team for use in other studies?

As part of this study, we are obtaining specimens and data from you. We plan to store and use these specimens and data for studies other than the one described in this consent form that are going on right now, as well as studies that may be conducted in the future. The specimens and data will be kept in a way that we will still know that they came from you (i.e., they will be identifiable to us). If we use your identifiable specimens or data for future research, our study will be reviewed and approved by an Institutional Review Board who will make sure that we are protecting your confidentiality. These future studies might help us better understand post transplant cytopenia(s), 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 identifiable specimens and data to be stored and used by the study team for future studies as described above.

_____ Yes _____ No

Initial Initial

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

We may share your specimens and data with other researchers. The other researchers may be doing studies in similar areas to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or at commercial entities.

If we do share your specimens or data, we will know that the specimens and data came from you. However, the other researchers will not know that they came from you (i.e., they will be de-identified).

I give permission for my **de-identified** specimens and data to be shared with and used by other researchers for future studies.

_____ Yes _____ No

Initial Initial

In some cases, it may help other researchers to know that the specimens or data were collected from you (i.e., they will have your identifiers). If we share your identity with other researchers, their study will be reviewed and approved by an Institutional Review Board who will make sure that the study team is protecting your confidentiality.

I give permission for my **identifiable** specimens and data to be shared with and used by other researchers for future studies.

_____ Yes _____ No

Initial Initial

In addition to the planned use and sharing described above, we might remove any labels from your specimens and data that might identify you (i.e., anonymize them), and use them or share them with other researchers for future studies at the NIH or other places. When we or the other researchers use your anonymized specimens and data for these projects, there will be no way to know that they came from you. We want to make sure that you understand that this is a possibility if you participate in this study. Once we do this, we would not be able to remove your specimens or data from these studies or prevent their use in future studies because we would not be able to tell which specimens or data belong to you.

Can you change your mind about use and sharing for future research?

If you change your mind and do not want us to store and use your specimens and data for future studies, you should contact the study team. 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 is already complete, the information from that research may still be used. Also, if the specimens and data have been shared already, it might not be possible to withdraw them.

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

Your specimens and data may be stored by the NIH indefinitely.

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 that no one will 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?

You will not receive compensation for participation in this study.

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

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

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.
- National Institutes of Health Intramural Institutional Review Board
- Qualified representatives from Rigel Pharmaceuticals, the pharmaceutical company that produces fostamatinib.

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.

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, Dr. Jamie Hur, DO; jamie.hur@nih.gov; 301-528-7128.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.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:

1. **A short form consent process has been used to enroll a non-English speaking subject or**
2. **An oral presentation of the full consent has been used to enroll a blind or illiterate subject**

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.