The Cleveland Clinic Foundation
Consent to Participate in a Research Study

Study title: CASE 2918: A Phase II Study of CPX-351 as a Novel Therapeutic Approach for Patients With Myelodysplastic Syndromes (MDS) after Hypomethylating Agent Failure

Sponsor: Cleveland Clinic Foundation, NCT03957876
Funding Source: Jazz Pharmaceuticals
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Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at the Cleveland Clinic (CC).

KEY INFORMATION

The following is a short summary of this research study to help you decide whether or not to be a part of this research study. More detailed information is included later on in this document.

What should I know about a research study?

- Someone will explain this research study to you.
- You can choose whether or not to take part.
- You can agree to take part and then later change your mind.
- Your decision whether or not to participate will not be held against you.
- You can ask all the questions you want before you decide.

What is the purpose, procedures and duration of this study?

We are asking you to take part in a research study because you a) have been diagnosed with myelodysplasic syndrome (MDS), a bone marrow disorders causing a decrease in red blood cells which may cause fatigue and tiredness and b) you've had prior treatment with azacitidine or decitabine (hypomethylating agents, HMAs) that has previously failed you. The purpose of this

study is to evaluate the effect of treatment with CPX-351 (an FDA approved drug for the treatment of certain kinds of acute myeloid leukemia (AML)) in patients with MDS while using a new tool to predict outcomes of patients following HMA failure. This approach is intended to gain a better understanding and insight into finding new opportunities for drug approvals in this setting.

CPX-351 is an investigational (experimental) drug for the treatment of myelodysplastic syndrome that works by delivering two chemotherapy medications (daunorubicin and cytarabine) together which are then concentrated into the bone marrow (the part of the body that makes blood cells). CPX-351 is experimental because it is not approved by the Food and Drug Administration (FDA) for the indication of myelodysplastic syndrome. This drug is approved by the Food and Drug Administration (FDA) for the indication of certain types acute myeloid leukemia.

You will receive the CPX-351 on days 1, 3 and 5 of the first cycle. After you finish your first round of treatment and based on your response you may be eligible for another 4 cycles of treatment. Your doctor will inform you if this is an available option for you when the time comes. Once you have finished treatment your doctor will continue to watch you for side effects and follow your condition for 1 year.

Your participation in the research will last about 18 months.

More detailed information can be found under the section labeled: "Information on the Research."

Why might you choose not to participate in this research study?

There may be discomforts, side effects, and risks to using CPX-351 treatment that we do not know yet. Sometimes during a study, the sponsor may learn new information about the study drug and the risks, which the study doctor/staff will tell you about in a timely manner. This new information might make you change your mind about being in the study. The study drug may not be better, and could possibly be worse than the usual approach for your cancer. Additionally, you may lose time at work or home and spend more time in the hospital or the doctor's office than usual. You also may be asked sensitive or private questions which you normally do not discuss.

More detailed information about the risks of this study can be found in the section labeled "Risks."

Why might you choose to volunteer for this study?

We cannot know if you will have any benefit as a result of your participation in the study; it is possible the study treatment may improve your condition, which may give you relief from some symptoms or improve your quality of life. However, it is possible that your condition could worsen. Your participation in this study will help to obtain information about treating subjects with myeloid dysplastic syndrome.

More detailed information about the benefits of this study can be found in the section labeled "Benefits."

What is the usual approach to my *myelodysplastic syndrome (MDS)*?
Some patients receive no therapy and only receive red blood cell transfusions as needed (this is called supportive care). For lower-risk MDS patients with anemia, doctors often prescribe erythropoietin-stimulating agents (ESAs) which help stimulate red blood cell production. For patients who do not respond or stop responding to ESA treatment, there are currently two types of FDA approved therapies that may be used: HMAs and lenalidomide (Revlimid). You may also be a candidate for a bone marrow transplant, which should be further discussed with your physician.

What are my other choices if I do not take part in this study?
If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer. For example: comfort/palliative care

More detailed information about the alternatives to this study can be found in the section labeled "Alternatives."

Do the researchers or institution have any conflicts of interest relating to this study?
One or more of the Investigators conducting this study serve as consultants for the company that makes products used in this study. These financial interests are within permissible limits established by the local institutional Conflict of Interest Policy. If you have any questions regarding conflicts of interest, please ask you study doctor or call the Cleveland Clinic Institutional Review Board at (216) 444-2924.

DETAILED INFORMATION

The following is more detailed information about this study in addition to the information listed above.

1. INFORMATION ON THE RESEARCH

Why is the research study being done?
The purpose of this study is to evaluate the efficacy of treatment with CPX-351 (an FDA approved drug for the treatment of AML) in patients with MDS while using a new stratification tool to predict outcomes of patients following HMA failure. This approach is intended to gain a better understanding and insight into identifying new opportunities for drug approvals in this setting.

CPX-351 is an investigational (experimental) drug for the indication of myelodysplastic syndrome that works by delivering two chemotherapy medications (daunorubicin and cytarabine)

together which are then concentrated into the bone marrow (the part of the body that makes blood cells). CPX-351is experimental because it is not approved by the Food and Drug Administration (FDA) for the indication of myelodysplastic syndrome. This drug is approved by the Food and Drug Administration (FDA) for the indication of acute myeloid leukemia.

How Many People Will Take Part in this Study?
Approximately 30 people will take part in this study at Cleveland Clinic.

What is involved if you decide to take part in this research study?
Prior to beginning the study you will have to agree to participate by signing this consent form. Upon signing consent, you will begin the screening period. The screening period begins the day you sign consent and can take place over a 28 day period leading up to dosing on day 1 (D1). During the screening period you will be assessed to determine if you meet eligibility for this study.

Assessments before you begin the study:
You will need to have the following tests and procedures to find out if you can be in the study:

- History and physical examination, questions about how you are feeling and treatments you have received.
- ECHO (echocardiogram)
- ECG (electrocardiogram)
- Blood tests for routing testing (about 2 tablespoons)
- Blood draw for future research purposes (including possible genetic analysis) at screening, cycle 1 day 35 and end of treatment (about 1/2 tablespoon)
- Bone marrow biopsy and aspirate

If you are determined eligible to participate in this study, you will then be grouped into one of two groups. Prior to beginning treatment, all eligible patients will be grouped into low risk versus high risk based on a stratification tool used to determine your disease. Group 1 will be low risk participants and group 2 will be high risk participants. All study participants will get the same study drug, CPX-351.

You will receive the CPX-351 on days 1, 3 and 5 of the first 35 day cycle as outlined in the study calendar. After you finish your first round of treatment and based on your response, determined by a bone marrow biopsy and blood draw, you may be eligible for another 4 cycles of treatment. Your doctor will inform you if this is an available option for you when the time comes. Once you have finished treatment your doctor will continue to watch you for side effects and follow your condition for 1 year.

What tests and procedures will I have if I take part in this study?

Informed consent:
The study doctor/staff will talk to you about the study and you will decide if you want to join.

This will be done during the Screening visit.

Review medical history:
You will discuss your current and past health with the study doctor/staff. This will be done during the Screening visit.

Review of medications:
You will talk with the study doctor/staff about any medicines you take. This will be done during the Screening, Treatment and Follow Up visits.

Physical examination:
The study doctor/staff will check your body for general health. This will be done during the Screening and Treatment visits.

Vital signs:
The study doctor/staff will take your pulse, temperature, and blood pressure. This will be done during the Screening and Treatment visits.

ECG (Electrocardiogram):

Sticky patches that are connected to a machine that shows the electrical activity of your heart, are placed on your chest, arms and legs. This will be done during the Screening visit and maybe during Treatment visits if your Study Doctor advises you need this test.

Blood draw/tests:
The study doctor/staff will draw blood from a vein in your arm. You may get a bruise or irritation at the place where the needle goes into your skin. Some participants may faint and, in rare cases, can get an infection.

Sometimes you will need to repeat a blood test.
Your blood will be used to check for:

- Your general health
- Disease evaluations
- How your body handles the study drug
- Pregnancy (if you are a female who could get pregnant.)
- Scientific Research
    - 10mL of your blood will be taken for exploratory studies

Bone Marrow Aspirate/Biopsy:

An area of bone (usually pelvis) will be made numb by injecting a local anesthetic, and then a needle will be inserted into the bone. A small amount of bone and bone marrow will be removed. The bone marrow aspirate/biopsy will be used for disease evaluations, as well as Scientific/Genetic Research. This will be done during Screening, Treatment and at the End of Treatment visit. If you were to complete this trial, it would be anticipated that you would have 3 bone marrow tests.

A calendar of all study procedures and when they will take place can be found on the next page.

Study Calendar

Period	Screening Period	Induction Phase							Consolidation Phase				End of Treatment (EOT)	Follow-up[g]
		1 cycle							Up to 4 cycles					
Day	28 Days	1	2	3	4	5	6-27	35[l]	1[dij]	2	3	4 - 28		
CPX-351 Administration[a]		X		X		X			X		X			
Informed Consent Form (ICF)	X													
Disease history and prior therapies	X													
History and physical exam[b]	X								X				X	
Vital signs[b]	X	X[op]		X[op]				X	X[op]		X[op]			
Concomitant medications	X	X							X				X	
ECOG performance status[cj]	X								X				X	
Hematology[b]	X	X	X	X	X	X	X[n]	X	X[e]			X[n]	X	X[g]
Serum chemistry[b]	X	X	X	X	X	X	X[n]	X	X[e]			X[n]	X	X[g]
Pregnancy test	X	X[k]							X[k]					
Echocardiogram	X[r]	X[q]							X					
Electrocardiogram	X[r]													
Bone marrow biopsy and aspiration[b]	X[r]							X					X	
Disease response assessment[f]	X							X					X	
Correlative analysis blood draw[m]	X							X					X	
Survival follow-up														X[h]
Adverse event assessment	← X →													

a: During the induction phase all patients will receive 44mg/m^2 on days 1, 3 and 5. Following the induction phase if patients achieve a response (per section 12.0) they may continue onto the consolidation phase. During the consolidation phase patients will receive 15.4mg/m^2 on days 1 and 3 (daunorubicin 15.4 mg/m^2 and cytarabine 35 mg/m^2) for up to 4 cycles.
b: See Appendix IV for required tests (available to the patient upon request).
c: See Appendix I for performance status grading (available to the patient upon request).
d: Indicates at +/-3 day window.
e: Required twice weekly to monitor counts, can be completed at a local laboratory.
f: See Section 12.0 for MDS response assessment criteria.
g: Follow up will occur monthly as standard of care (SOC) for the first 6 months of follow-up. See section 6.4 for adverse event reporting requirements.
h: Survival Follow up will occur bimonthly (60 days) for a duration of 1 year from patient's EOT visit.
i: During only the first cycle in consolidation phase, CPX-351 must be given no earlier than 35 days after the start of induction and no later than 75 days after the start of induction. There should be 35 days between the start of each subsequent consolidation cycles Patients must have recovered to Absolute neutrophil count (ANC) >500/μL and platelets >50,000/μL to be eligible for any consolidation therapy.
j: Prior to the first cycle of consolidation therapy, patient must have a performance status (ECOG PS)(determined by physician based on physical ability) of 0-2.
k: Must be negative prior to dosing
l: Indicates a +/-10 day window.
m: 10mL of whole blood will be collected in an extra lab tube and stored for future research testing (specific tests to be run are unknown at this time).
n: Hematology and serum chemistry will be assessed 1-3x weekly at the discretion of the treating physician to monitor counts. These can be completed at a local laboratory.
o: On dosing days, for induction phase only, vitals must be collected prior to infusion, 5, 10, 30 and 60 minutes post the start of infusion and at the end of infusion. On dosing days, for consolidation phase, vitals must be collected prior to infusion and at the end of infusion.
p: Indicates a (+/-) 5 minute window.
q: Required if patient has not had an ECHO within 28 days of C1D1.
r: If completed prior to consent and within 28 days of C1D1, may count towards screening procedures.

Scientific Research
At the screening, C1D35 and end of treatment visit an extra 10mL (about 2 tablespoons) of blood (correlative analysis blood draw) will be collected for future research studies that are unknown at this time.

How will be samples for scientific research be used?
Your samples collected for this research will be analyzed for the study. As part of the analysis, the research might include whole genomic sequencing. This means that researchers may look at your sample to learn about your genes (DNA). There are different ways to look at your DNA. Researchers often use a technology called sequencing to look at your DNA. Sequencing "reads" each letter of the DNA and finds changes (also called "variations" or "mutations") in your genes that may cause disease or affect how your body reacts to a certain disease.

The research done with your blood may lead to the development of new products in the future. You will not receive, either now or in the future, any compensation, royalty, or other financial benefits resulting from any product, procedure, or other items developed from studying your sample(s).

Will I be notified of the results of the tests/studies on my samples?
The tests/studies described are for research purposes only. It is not the purpose of these tests/studies to look for or provide you with any medical information or diagnoses relating to your present condition or any other disease or illness. Therefore, you will not receive results from these research tests/studies.

2. ALTERNATIVES

What are the alternatives to participation in the research study?

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer. For example: comfort/palliative care

What is the usual approach to my myelodysplastic syndrome (MDS)?
Some patients receive no therapy and only receive red blood cell transfusions as needed (this is called supportive care). For lower-risk MDS patients with anemia, doctors often prescribe erythropoietin-stimulating agents (ESAs) which help stimulate red blood cell production. For patients who do not respond or stop responding to ESA treatment, there are currently two types of FDA approved therapies that may be used: HMAs and lenalidomide (Revlimid).

3. RISKS

What are the risks of participating in the research study?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- There is a potential risk that this study may delay or prevent the ability to use bone marrow transplant as a subsequent therapy, or may impact the outcome of that therapy.

The chemotherapy used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug(s)/study approach.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible side effects of CPX-351 are listed below.

COMMON, SOME MAY BE SERIOUS

In 100 people receiving CPX-351 more than 20 and up to 100 may have:

- Abdominal pain
- Anemia
- Anxiety
- Arrhythmia
- Ataxia (impaired muscle control of walking, picking up objects, etc.)
- Chest pain
- Chills
- Constipation
- Cough
- Decreased appetite
- Delirium
- Diarrhea
- Dizziness
- Dyspnea (Shortness of breath)
- Edema
- Extravasation tissue injury (unintentional leakage of IV fluid into surrounding skin causing tissue injury and or tissue death)
- Fatigue
- Febrile neutropenia (Fever with low neutrophil counts in the blood)
- Fungal infection
- Headache
- Hemorrhage
- Hypertension
- Hypotension
- Hypoxia (Low oxygen levels in the blood)
- Rash
- Mucositis (Inflammation and sores of the mouth)
- Musculoskeletal pain
- Nausea
- Neutropenia (Low neutrophil counts in the blood, which leads to increased risk of infection)
- Non-conduction cardio toxicity (Damage to the heart, which can lead to heart failure)
- Pleural effusion (Water in the lungs)
- Pneumonia
- Pruritus (Itching)
- Pyrexia (Fever)
- Rash
- Skin peeling (especially palms of hands and soles of feet)
- Sleep disorders
- Vomiting

OCCASIONAL, SOME MAY BE SERIOUS
In 100 people receiving CPX-351, from 4 to 20 may have:
▪ Acute renal failure or renal insufficiency, which can be so severe as to lead to a need for dialysis. ▪ Cellulitis (infection in the skin and deeper tissues ▪ Catheter/injection site reaction ▪ Ejection fraction decreased (Diastolic heart failure) ▪ Fatigue ▪ Hemorrhoids ▪ Hypokalemia (Low potassium in the blood) ▪ Progressive cancer – malignant neoplasm progressive (uncontrolled growth of tumor cells) ▪ Petechiae (bleeding spots in the skin) ▪ Pneumonia ▪ Pyrexia ▪ Rash ▪ Sepsis (Infection in the blood) ▪ Urinary tract infection ▪ Respiratory failure, even to the point of needing to be connected to a breathing, or life support machine in an intensive care unit. ▪ Transfusion reactions ▪ Upper respiratory induction (excluding fungal) ▪ Visual impairments (except bleeding, and eye pain)

Reproductive Risks

There may be unforeseen risks to an unborn child associated with your taking CPX-351. Therefore, if you are capable of giving birth to or fathering a child, you and your sexual partner should use adequate birth control measures while you are in the study. These measures may include abstinence, oral contraceptives (birth control pills), IUD, diaphragm, approved hormone injections, condoms, or documentation of medical sterilization. Discuss with your doctor which birth control measures are acceptable.

If you are unwilling to do this, we ask that you not participate in this study. Pregnancy tests will be performed on all women of child-bearing potential before beginning the study and during the study approximately every 4 weeks. If you or your sexual partner become pregnant while taking part in this study you must notify the study doctor immediately.

Blood Draws

The insertion of the needle to draw blood can be painful; however, the discomfort is brief. For most people, needle punctures to get blood samples do not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting. Most subjects will have a central catheter (Hickman catheter), and most blood tests can be drawn through it.

Bone Marrow Biopsy
There are also risks associated with taking samples of your bone marrow. Your study doctor or his/her designee will insert a needle into your hip or breast bone to withdraw a sample of fluid containing bone marrow cells. The risks of bone marrow sampling commonly include discomfort, pain, redness, swelling, and/or bruising where the sample is taken from your hip or chest. Sometimes bleeding can occur at the place where the sample is drawn. Fainting and infection can happen, but rarely. Many patients also experience soreness or stiffness in the hips for several days after the procedure.

Electrocardiogram (ECG)
Some people's skin reacts to the sticky patches that attach the electrodes to the chest for the ECG. This skin irritation usually disappears when the patches are removed. Some men may have some chest hair shaved

HIV Testing
As a part of this study, a sample of your blood is being tested for the presence of HIV (Human Immunodeficiency Virus). HIV is the virus that causes AIDS (Acquired Immunodeficiency Syndrome). If your blood test is positive and you live in the State of Ohio, the result and your demographic information will be reported to the Ohio Department of Health as is required by law. In addition, this information will be available on the hospital's laboratory reporting system. The results may influence your insurability and/or employability regarding your health status. If you test positive for HIV or active hepatitis B or C you will not be eligible to participate in this study.

Infectious Disease Testing
As a part of this study, a sample of your blood is being tested for the presence of hepatitis. If your blood test results are positive and you live in the State of Ohio, the results of that test, if positive, and demographic information about you will be reported to the Ohio Department of Health as is required by law.

Unknown Risks
There may be risks or side effects related to the study drugs that are unknown at this time. You will be notified of any significant new findings that become known that may affect your willingness to continue in the study.

Confidentiality Risks
There is a potential risk of loss of confidentiality of your data. Efforts will be made to keep your information confidential through the use of the following safeguards: use of codes, storage in a password protected computer accessible only by the research team**.** If you decide to be in this study, the study researchers will get information that identifies you and your personal health information. This may include information that might directly identify you, such as your name and address. This information will be kept for the length of the study. After that time it will be destroyed or de-identified, meaning we will replace your identifying information with a code that does not directly identify you. The principal investigator will keep a link that identifies you to your coded information, but this link will be kept secure and available only to the principal investigator or selected members of the research team. Any information that can identify you

will remain confidential. Any personal information that could identify you will be removed or changed before files are shared with other researchers or results are made public.

Genetic Risks
Your medical and genetic information is unique to you. There is a risk that someone outside of the research study could get access to your study records or trace information in a database back to you. They could use that information in a way that could harm you. While the chance that someone could access and misuse your information is believed currently to be very small, it is possible that the risk may increase in the future as people find new ways to access information.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), effective May 21, 2010, generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

4. BENEFITS

What are possible benefits of participating in the research?
We cannot know if you will have any benefit as a result of your participation in the study; it is possible the study treatment may improve your cancer, which may give you relief from some symptoms, improve your quality of life or prolong your survival. However, it is possible that your condition could worsen. Your participation in this study will help to obtain information about treating subjects with MDS. Your participation in this study may provide information that may help other people who have a similar medical problem in the future.

5. COSTS

Are there any costs to you if you participate in this study?
Your involvement in this research study is voluntary and you will not be paid for your participation.

The study agent, CPX-351 will be provided free of charge by Jazz Pharmaceuticals, while you are participating in this study. Neither you nor your insurance provider will be responsible for the costs of any research-only tests or procedures. Some blood work tests and echocardiograms for research purposes will not be charged to you. It will be paid for by the research study.

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study (i.e., medical history, review of medications, physical exams, performance status, routine blood tests, pregnancy test, hospitalizations, x-rays and/or scans for tumor measurement). Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

6. RESEARCH RELATED INJURY

What will happen if you are injured as a result of taking part in the research?

In the event you suffer a research related injury as a result of being in this study, Cleveland Clinic will provide appropriate medical treatment for such injury in a timely manner. Provision of such medical treatment does not imply any negligence or other wrongdoing on the part of Cleveland Clinic or any of the physicians or other personnel involved in the study. If you believe that you have been injured as a result of participating in the study, please immediately contact your Cleveland Clinic study doctor even if you may have already been seen or treated by another doctor. If you are seen or treated by a doctor other than the study doctor, you should inform such doctor that you are in this study and, if possible, take this document with you as it may help such doctor treat you.

In the event you suffer a research related injury as a result of being in this study, the costs for medical treatment may be billed to you or your medical insurance plan, if applicable. Medical insurance plans may or may not cover costs for medical treatment of research-related injuries. If you have insurance, you should check with your medical insurance plan before deciding to participate in this research study. In the event your medical insurance plan covers some or all of the treatment costs, you may still be responsible for co-pays or deductibles as required by your medical insurance plan.

Cleveland Clinic has not set aside any money to pay you or to pay for your treatment if you suffer a research related injury as a result of being in the study. There are no plans for Cleveland Clinic to provide other forms of compensation (such as lost wages, pain and suffering, or other direct or indirect losses) to you for research related injuries. You are not waiving any legal rights by signing this form, including the right to seek compensation for an injury. Further information about research related injury is available by contacting the Institutional Review Board at (216) 444-2924.

7. PRIVACY AND CONFIDENTIALITY

What will happen to your information that is collected for this research?

Cleveland Clinic may share your study information, without anyone knowing that it is related to you specifically, with others or use it to research projects not listed in this form. Your blood samples may be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If

your identifying information is removed from your blood samples, we will no longer be able to identify and destroy them.

Study results may be shared in medical journals, at scientific meetings, and in other media without your identifying information. Your records will be confidential and your identity will not be shared in medical journals, at scientific meetings, and in other media without your express consent.

Authorization to Use/Disclose Protected Health Information

Cleveland Clinic has rules and procedures to protect information about you. Federal and State laws also protect your privacy.

The research team working on the study will collect information about you. This includes your health information, data collected for this research study and personal identifying information including your name, address, social Security number, date of birth and other identifying information.

Generally, only people on the research team will know your identity and that you are in the research study. However, sometimes other people at Cleveland Clinic may see or give out your information. These include people who review research studies including the Institutional Review Board and Research Compliance, their staff, lawyers, or other Cleveland Clinic staff.

People outside Cleveland Clinic may see your information for this study. Examples include government groups (such as the Food and Drug Administration), safety monitors, other hospitals in the study and the sponsor of the research, their agents, and Jazz Pharmaceuticals. Cleveland Clinic will take steps to ensure your information is kept confidential and that only the health information which is minimally required to conduct the study is used or disclosed to people outside Cleveland Clinic; however, people outside Cleveland Clinic who receive your information may not be covered by this promise.

You do not have to give this permission to use and give out your information; however you will not be able to participate in this research study without providing this permission by signing this consent form. The use and disclosure of your information has no expiration date.

You may cancel your permission to use and disclose your information at any time by notifying the Principal Investigator in writing at:

Sudipto Mukherjee, MD, MPH
Cleveland Clinic Foundation
9500 Euclid Avenue
Mail Code: CA-6
Cleveland, OH 44195

If you do cancel your permission to use and disclose your information, your participation in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in the study.

The Genetic Information Nondiscrimination Act (GINA) is a federal law designated to protect you from health insurance and employment discrimination based on genetic information. It is illegal for health insurance providers and most employers to ask for genetic information to make decisions about a person's eligibility or coverage or to make employment decisions.
The law will not stop health insurance companies from using genetic information to decide whether to pay claims and also does not apply to life insurance, disability insurance or long-term care insurance.

Clinical Trials Language
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U. S. law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search the Website at any time.

8. QUESTIONS

Who do you call if you have any questions or problems?
If you have any questions or concerns about the research, or develop a research-related problem, you should contact the Principle Investigator and/or research staff at (216) 445-7009. During non-business hours, weekends and holidays, please contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the oncologist (cancer doctor) that is on call. . If you have questions about your rights as a research subject, you should contact the Institutional Review Board at (216) 444-2924.

9. VOLUNTARY PARTICIPATION
What are your rights as a research participant?

Taking part in this study is voluntary. You will be told of any new, relevant information from the research that may affect your health, welfare, or willingness to continue in this study. You may choose not to take part or may leave the study at any time. Withdrawing from the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to withdraw from the study you should discuss with your study doctor your decision to ensure a safe withdrawal.

If you leave the study early, Cleveland Clinic may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:
- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study requirements
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or FDA.

If you become pregnant.

10. SIGNATURES

Statement of Participant

I have read and have had verbally explained to me the above information and have had all my questions answered to my satisfaction. I understand that my participation is voluntary and that I may stop my participation in the study at any time. Signing this form does not waive any of my legal rights. I understand that a copy of this consent will be provided to me. By signing below, I agree to take part in this research study.

_____
Printed name of Participant

_____ _____
Participant Signature Date

_____ _____ _____
Signature of Witness Date Printed Name of Witness
I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study. *(Only required when a witness is used in the consenting process).*

Statement of Person Conducting Informed Consent Discussion

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____
Printed name of person obtaining consent

_____ _____
Signature of person obtaining consent Date