PRINCIPAL INVESTIGATOR: Alain Mina, MD

STUDY TITLE: A Phase I/II Trial of Eltanexor (KPT-8602) with Inqovi (Decitabine-Cedazuridine) in High-Risk Myelodysplastic Syndromes

STUDY SITE: National Institutes of Health (NIH), Clinical Center (CC)

Cohort: Affected Participant

Consent Version: 10/30/2024

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.

You are being asked to take part in this study because you have a high risk Myelodysplastic Syndrome (HR-MDS) that did not respond to treatment.

The main purpose of the phase I part of this research study is to test the safety of different doses of the drug KPT-8602 (eltanexor) in combination with decitabine-cedazuridine (Inqovi®), and to determine the safest dose for participants with MDS. The main purpose of the phase II part of the study is to determine if this combination of drugs works together to treat MDS.

KPT-8602 is an "investigational drug", which means it is not approved by the U.S. Food and Drug Administration (FDA) for the treatment of any disease. Although Inqovi has been approved by the FDA to treat MDS, the use and combination of the drugs in this study is investigational.

There are other drugs and treatments that can be prescribed by your regular cancer doctor if you are not in this study. These drugs all work in different ways compared to the study drugs, and with different side effects.

If you prefer other drugs or treatments, you should consider not joining the study. Some of these treatments are:

- other drugs in the same class as Inqovi, such as azacitidine or decitabine,
- other oral treatments such as lenalidomide, or
- drugs that would not treat the disease directly but may help improve your blood counts and overall symptoms, such as erythropoietin stimulating agents.

If you decide to join this study, here are some of the most important things that you should know that will happen:

- First, we will perform tests to find out if you fit the study requirements – this is called "screening". This will involve a check of your health history, a physical exam, and having standard blood tests, scans, and test of your heart. You also may have a bone marrow biopsy to confirm your diagnosis of MDS if unable to confirm by obtaining an outside bone marrow sample. Screening involves only standard clinical tests, so we do not think you may experience serious side effects during screening. The screening portion of this study will take about a week.
- In the first part of the study (phase 1), we want to find out the highest dose of KPT-8602 that is safe to use with Inqovi. We will test increasing doses of KPT-8602 with fixed dose Inqovi in small groups of participants. If you were already on Inqovi before the study, you will continue this medication at the same dose. We also want to find out what kind of side effects these medications might cause. After the first part is done, we will enroll additional participants in a second part of the study (phase 2) to learn more about whether these study medications effectively treat your disease.
- The study drugs will be given as follows in cycles of 28 days.
    - Participants with HR-MDS will take the following by mouth once a day:
        - Inqovi on days 1-5 of each cycle.
        - KPT-8602 either on days 8-12 and days 15-19 or days 8-21 (depending on the assigned dose level) of each cycle.
- You will continue these 28-day cycles for as long as you are handling the medication well, as long as your disease is not getting worse, and as long as you would like to continue being in the study. However, if we do not observe (at least) less cancer in your body (partial remission), you will stop taking study drugs after 6 cycles.
- You may have side effects from taking part in this study. Some can be mild or very serious, temporary, long-lasting, or permanent, and may include death. Examples of some of the side effects that you may have include:
    - changes in blood counts (such as low red or white cells),
    - diarrhea, nausea and/or vomiting,
    - rashes,
    - fatigue, and
    - infections.

Since this is the first time that these drugs are being given together, there may be side effects that we cannot predict.

- You will have regular visits to the Clinical Center during your participation in the study. You will have bone marrow biopsies and other laboratory testing to see how you are doing and to see if the study drugs are having any effect on your disease. We will also collect research samples from you (including blood, and bone marrow) so we may better understand your disease and how well the study drugs are working.

- After you stop taking the study drugs, you will come to the NIH Clinical Center (or you will see your regular oncologist) periodically for up to about 8 years. This is to assess your health and to determine what impact, if any, the study drugs may have had on your disease.
- Because of the chance of potential harm to an unborn child, if you are capable of becoming pregnant or the partner of a person who may become pregnant you MUST use birth control from the time you start study drug, throughout the study (including interruptions in taking the study drugs), and for 6 months after the last dose of study drug.

We do not know what side effects you might have. We do not know if you will benefit from taking part in this study. The potential benefits could include improvement or lessening of your symptoms, caused by your disease. If you do not benefit, this study and the results from our research may help others in the future.

You are free to stop being in the trial at any time. If you decide to stop, the study doctor may ask you to have 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 interventions in which they would want to participate. 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.

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?

You are being asked to take part in this study because you have a high risk Myelodysplastic Syndrome (HR-MDS) that did not respond to treatment.

The main purpose of the phase I part of this research study is to test the safety of different doses of the drug KPT-8602 (eltanexor) in combination with decitabine-cedazuridine (Inqovi®), and to determine the safest dose for participants with MDS. The main purpose of the phase II part of the study is to determine if this combination of drugs may work together to treat MDS.

KPT-8602 is an "investigational drug", which means it is not approved by the U.S. Food and Drug Administration (FDA) for the treatment of any disease. Although Inqovi has been approved by the FDA to treat MDS, the use and combination of the drugs in this study is investigational.

WHAT WILL HAPPEN DURING THE STUDY?

Before you begin the study

Before beginning the study, you will need to undergo tests and/or procedures to see if you are eligible to take part. This is called screening. All of these tests or procedures are part of your

regular care. If you have had some of these tests or procedures recently, they may or may not have to be repeated. The following tests and procedures are needed to determine whether you are eligible for this trial:

- Medical history: A complete review of your medical history, including obtaining information about your diagnosis and previous treatments, and reviewing information about your other conditions. If you have medical records from another clinic or hospital, you will be asked to get copies of these records, or your study doctor may be able to request them on your behalf.
- Physical exam: This will include taking your height, weight, vital signs (temperature, blood pressure, heart rate, breathing rate), seeing how you function in your daily activities, any current symptoms of your condition and a review of all medications that you take.
- Standard blood tests:
    - Tests to measure your liver, kidney, white blood cells, red blood cells and platelets, blood electrolytes and how well your thyroid functions
    - If you are able to get pregnant and you are not already known to be pregnant, you will also have a pregnancy test done. This may be done by blood or urine test. You will not be able to participate if you are pregnant.
    - To check for Hepatitis B and C infection
    - To check for HIV infection: 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 active/uncontrolled HIV or are currently taking medications for 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
- An electrocardiogram (ECG) of the heart will be done to check the electrical activity and the function of your heart You will need to lie still for about 5 minutes. We will place electrodes on your chest, arms, and legs. Electrodes are small stickers that are attached to wires that go to the machine. The electrical signals are transmitted to the a machine so we can review a print out of your heart rhythm.
- A bone marrow biopsy may be performed to confirm your diagnosis of MDS if we were unable to confirm your diagnosis by obtaining an outside bone marrow sample.
    - We may ask you to have a bone marrow biopsy and aspiration to collect bone marrow tissue and cells from your hip. Bone marrow is the soft material in the center of bones that makes new blood cells. The area will be numbed with lidocaine and once numb, a large needle will be inserted through a small cut in your skin. Then we will take about 4 tablespoons or specify alternative volume as relevant of marrow out of your bone. *We may also take a small piece of bone.* We will check your pain level during the procedure. We want you to tell us how you are doing. We may give you more numbing medicine if you need it. The procedure will take about 1 hour to complete. *We will call you about 2 days later to see how you are doing.*

- Some genomic studies may be performed on blood or bone marrow samples if needed to confirm diagnosis

Before you begin the study therapy

If the screening tests show that you are eligible to take part and if you choose to be in it, you may need to have a few additional standard tests done if they haven't already been done recently. If any of the screening tests need to be repeated and show that you have become ineligible to be in the study, you will not be able to continue with this study.

Study Intervention

Study drugs will be given in a series of cycles. Each cycle is 28 days long.

In order to see if the dose of KPT-8602 together with Inqovi is safe, we will test the doses in 2 different groups of participants with high risk MDS (HR-MDS). Participants will be enrolled and start taking the study drugs in groups as follows:

- Phase 1: First, a group of 3-6 study participants will get Inqovi, at a fixed dose together with KPT-8602 at the starting dose. The dose of KPT-8602 will be escalated (or increased) in a new group of 3-6 patients, as long as there are no safety issues in the first group. If there are no safety issues in the second group, the dose of KPT-8602 will be increased again in ongoing groups of 3-6 patients for as long as it is safe to do so, and until the best or highest dose of KPT-8602 is found. We will monitor each group of participants closely for side effects at least 28 days before enrolling the next group and/or moving on to the next doses.
- Phase 2: Once the highest safe dose of KPT-8602 given together with Inqovi is found, then the next part of the study will begin. In this part of the study, participants will get the safest doses of the study drugs as determined in the phase 1 part of the study so we can learn more about this drug combination and its effect on MDS.

The study drug schedule is described in more detail here:

- You will take the following by mouth once a day:
  - Inqovi on days 1-5 of each cycle (unless you have been assigned to a lower dose level).
  - KPT-8602 either on days 8-12 and days 15-19 or days 8-21 (depending on the dose level you are assigned to) of each cycle.

Your dose of KPT-8602 will be assigned depending on what dose level is open when you join the study, or depending on the safe dose found in phase 1 if you join during phase 2. You will get a fixed dose of Inqovi, on days 1-5 of each cycle. If you were already on a fixed dose of Inqovi prior to enrolling in this study, this medication will be continued at the same dose.

You will get a supply of each of the oral medications to take at home. During the first cycle of study drugs, you will return to the clinic for blood draws on day 8, and on day 12 or day 21 (depending on the dose level you are assigned to). On the days you are being seen in clinic, you must bring in your medication supply from home. You should not take your medication until we tell you to, because the blood draws must be timed with when you take the study drugs.

On the days you are not being seen in the clinic, take each of the oral drugs at about the same time each day. Do not break, crush, or divide KPT-8602 tablets, because that could cause a reaction from the powder touching your skin. Take KPT-8602 with food or within 30 minutes of eating. Swallow the Inqovi tablet whole, and do not crush, cut, or chew the tablet. Take Inqovi on an empty stomach, 2 hours before or 2 hours after meals. If you miss a dose of your medication within 12 hours of the time you usually take it, take the missed dose as soon as possible and then resume your normal dosing schedule the next day. Extend the dosing period by 1 day for every missed dose to complete the total number of doses for each cycle. If you are in the phase I study or on a staggered dosing schedule and missed a dose, contact the study team for further dosing instructions. However, if you vomit a dose of medication, do not take an additional dose, just continue with the next scheduled dose.

We will ask you to bring any leftover study drugs to each clinic visit. You will be given a drug diary to help you remember the schedule and to record each dose that you take. We will ask you to bring this diary to each clinic visit.

Certain medications need to be used with caution while you are participating on this study. If any physician other than the study team prescribes a medication for you for another condition, or you plan to take any new over-the-counter medications, vitamins or herbal supplements, you must check with us before starting. This is important because the interaction of some medications may cause serious side effects and/or may still be unknown. Your study team will discuss with you what medications to avoid during your study participation.

You will continue these 28-day cycles for as long as you are handling the medication well, your disease is not getting worse, and you would like to continue taking the study drugs. However, if we do not observe (at least) less cancer in your body (i.e., partial remission), study drugs will be stopped after 6 cycles.

Study Procedures

Similar to the tests done at the beginning of the study to see if you were eligible to join the study, the following procedures will be done to see if you are having side effects or if you are responding to the study drugs. Also, we may recommend additional testing (beyond what is listed below) at other times if needed.

Clinical Assessments and Procedures:

- History and physical exam, including obtaining information about side effects and symptoms, and a review of your medications: before starting study drug, before the start of every cycle, on Day 8 of Cycle 1, Day 15 of Cycles 1-3 and Day 22 of Cycle 1 and when you stop taking study drugs.
- Questions about how how you function in your daily activities: before starting study drugs and before the start of every cycle.
- Vital signs taken before starting study drug, before the start of every cycle, and on Days 8, 15 and 22 of Cycle 1, and on Days 1 and 15 of cycles 2-3, and when you are done taking the study drug.

- Standard blood tests : before the start of every cycle, on Day 8 of Cycle 1, Day 15 of Cycles 1-3 and Day 22 of Cycle 1 and at the end of taking the study drug and when/if your disease gets worse (unless noted otherwise below):
    - Tests to measure your liver and kidney function, white blood cells, red blood cells and platelets, and blood electrolytes
    - If you are able to get pregnant and you are not already known to be pregnant, you will also have a pregnancy test done before starting the study, and before the start of every cycle (this may be done by blood or urine test).
    - Tests to see how well your blood clots only when/if your disease gets worse
    - Tests to measure the amount of different types of white blood cells (part of your immune system before starting study drugs, before the start of every cycle and when/if your disease gets worse
- Standard urine sample: before starting study drugs, before the start of every cycle, and at the end of taking study drugs.
- An electrocardiogram (ECG) of the heart will be done to check the electrical activity and the function of your heart before starting study drugs, on Day 1 and 15 of Cycle 1 and as needed. Once the electrodes are placed, the test will begin, is completely painless, and generally takes less than a minute to perform. After the test, the electrodes are removed.
- Questionnaires to see how you are doing (for English-speakers; may be done electronically): before starting study drugs, weekly through Cycle 3, at the end of each subsequent cycle, at disease progression, end of treatment, and post-therapy follow-up. These will take approximately 30-40 minutes to complete.
- A bone marrow aspiration and/or biopsy will be done before starting study drugs, on Day 28 of Cycle 1 for Phase 1 participants only, on Day 28 of Cycles 2 and 6 for Phase 2 participants only, when/if your disease gets worse. These samples will also be used for additional research testing.

Additional research testing

In addition to the tests that we will conduct to determine whether you are having side effects or if you are responding to the study drugs, we will also collect samples from you for research. Some of these samples will be collected and stored for future use. In addition, any unused biological sample or derivative taken from you during this study may be used for research and/or stored for future research purposes.

- Blood Samples:
    - Blood will be collected: before starting study drugs, at the start of every cycle, at disease progression and/or end of treatment.
    - Pharmacokinetic (PK) (the movement of drugs through the body) and pharmacodynamic (PD) (the body's biological response to drugs) blood samples will be collected to look at levels of some of the study drugs in the body. These samples would be done as follows, for both Phase 1 and 2 participants: Several times on day 8 (up to 24 hours after receiving study

drugs on that day), and either Day 12, or 21 of cycle 1 depending on what dose level you are assigned to (up to 48 hours on those days). Additional samples will be taken before taking the drug dose on Day 15 of cycles 2 and 3.

- Bone marrow samples: As listed above in the Study Procedures section.

The following sections describe studies to be done on your samples for research:

What tests will be done on my samples?

All of your samples collected for research purposes on this study (such as the cancer cells from peripheral blood/bone marrow samples and normal tissue) may be used to look for specific changes in the DNA in tumors that could be used to develop new ways of diagnosing and treating cancer. DNA (also called deoxyribonucleic acid) in the cells carries genetic information and passes it from one generation of cells to the next – like an instruction manual. Normal tissue contains the DNA (instructions) that you were born with, DNA in cancer cells has changed – or mutated – and we think that change in the DNA is what causes tumors to form and to grow.

To look at your DNA, we may do what is called "whole genome sequencing." This is where we will do special tests in the lab to look at the entire sequence, or order, of how your DNA is put together. This is what makes you unique.

To determine which parts of the DNA have mutated, we will compare the DNA in your cancer cells to DNA from your normal cells. We will then analyze the results from similar cancers to see if there are any changes in the DNA that are common to a particular type of tumor. To examine the tumor and normal tissue we may use several different techniques depending on the type of tissue we collect. These could include growing cell lines (cells which keep dividing and growing in the laboratory, sometimes for years allowing us to continually study those cells), xenograft studies (placing or growing cells in another animal, such as mice), and looking in detail at the parts of the genes that produce specific proteins.

However, you should know that the analyses that we perform in our laboratory are for research purposes only; they are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing or testing for routine clinical care. For these reasons, we will not give you the results of the research tests done on your research samples in most cases. There may be exceptions to what we share with you and this is described later in this consent form in the section for "Return of research results."

When you are finished taking the drugs

You will be asked to return to the clinic about 30 days after the last dose of study drug. After this time, follow up will occur via phone call every 3 months for first 24 months, then every 6 months for 3 years, then annually for up to 8 years post enrollment to see how you are doing. If you are no longer being seen at the NIH during this time, we may request copies of your medical records from your outside providers.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, the screening portion is expected to take about one week. If you are eligible to take part, your involvement is expected to last for as long as you are responding

to the study drugs and do not have an unacceptable side effect. We will also continue to follow you by phone call after you stop taking the study drugs, for up to 8 years from starting the study.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 73 people participate in this study at the NIH.

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

If you choose to take part in this study, there is a risk that the study drugs may not be as good as regular treatment at shrinking or stabilizing your cancer. The study drugs may not be able to shrink or stabilize your cancer.

The drugs 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 test your blood and will let you know if changes occur that may affect your health.

Here are important things to know 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, and some may never go away.
- Some side effects may make it hard for you to have children.
- Some side effects may be mild. Other side effects may be very serious and even result in death.

You can ask your study doctor questions about side effects at any time. Here are important ways to make side effects less of a problem:

- If you notice or feel anything different, tell your study doctor. He or she can check to see if it is a side effect.
- Your study doctor will work with you to treat your side effects.
- Your study doctor may adjust the study drugs to try to reduce side effects.

Risks and side effects related to the study drugs and the procedures on this study are identified below:

KPT-8602

Likely:

- Nausea
- Fatigue
- Diarrhea
- Decreased appetite
- Low platelet count (cells that help blood to clot) (thrombocytopenia)
- Weight loss
- Low red blood cell count (anemia)
- Vomiting

- Low white blood cell count (cells that help fight infection) (neutropenia)
- Hyponatremia (low sodium levels)

Less Likely:

- Acute kidney injury
- Sepsis (a massive inflammatory response to an infection)

Decitabine and Cedazuridine:

Side effects include low blood counts (symptoms include fever, anemia, or bleeding) and increased risk of infection.

The most common side effects reported, include:

- Fatigue
- Constipation
- Hemorrhage
- Muscle pain (Myalgia)
- When your mouth or gut become sore or inflamed (Mucositis)
- Joint pain (Arthralgia)
- Nausea
- Shortness of breath (Dyspnea)
- Diarrhea
- Rash
- Dizziness
- Fever while white blood cells count is low (Febrile neutropenia)
- Edema
- Headache
- Cough
- Decreased appetite
- Upper respiratory tract infection
- Pneumonia
- Liver enzymes (Transaminase) increased

Risks from tests and procedures

- Blood draws: The possible side effects of drawing blood include pain, bleeding, bruising, dizziness, light-headedness, fainting and, on rare occasions, local blood clot formation or infection with redness and irritation of the vein. Up to 5.5 tablespoons of blood may be collected at one time, no more than 1 cup will be collected over an 8-week period.
- Bone marrow aspiration / Biopsy: The bone marrow aspiration and biopsy may cause pain, bruising, bleeding and infection. Soreness near the site may last for a couple of days after the procedure. You may have more pain, risk of bleeding and bruising if you complete both aspiration and biopsy rather than just the aspiration. If your pain is severe or you develop a fever, please contact the study team immediately.
- ECG: Some skin irritation can occur where the ECG electrodes are placed.

- Urine collection: There are no side effects associated with collection of urine.
- Questionnaires: Some of the questions in the questionnaire may be upsetting or make you feel uncomfortable. You can skip any of the questions you do not want to answer, and you can stop at any time.

You also may have the following discomforts:

- Spend more time in the hospital or doctor's office.
- Be asked sensitive or private questions about things you normally do not discuss.
- May not be able to take part in future studies.

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 taking the study drugs, and for 6 months after you finish taking study drugs. 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 study drugs b 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 while you take the study drugs and for 6 months after you finish the study drugs. 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.

Risks of returning secondary genetic findings

- The evaluation for unexpected gene changes is limited and may not be as complete as clinical genetic testing that might be available to you outside of the research study.
- If an unexpected gene change result is confirmed, then that test result will go into your NIH medical record. These documents are confidential, but other NIH investigators can see them.
- Learning about the changes in your genes could mean something about your family members and might cause you or your family distress. Before joining the study, it may be helpful to talk with your family members about whether they want you to share your results with them.
- If a gene change is found, it may reveal whether a particular parent passed on the change to a biological child.
- You may receive a result for an unexpected gene change that turns out not to cause that health condition. This may cause you unnecessary distress or lead to unnecessary medical testing risks and costs.

Protections against misuse of genetic information

This study involves genetic testing on samples. Some genetic information can help predict future health problems of you and your family and this information might be of interest to your employers or insurers. The Genetic Information Nondiscrimination Act (GINA) is a federal law that prohibits plans and health insurers from requesting genetic information or using genetic information. It also prohibits employment discrimination based on your health information. However, GINA does not address discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed condition or disease that has a genetic component.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You might not benefit from being in this study.

However, you may gain clinical information about your disease or your organ function that will be helpful to your overall medical care. The potential benefits could include lessening of your symptoms, such as pain, that are caused by MDS, reducing your cancer burden and improving your blood counts.

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

In the future, other people might benefit from this study because the knowledge gained from this study may help others in the future who have MDS.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

Before you decide whether to be in this study, we will discuss the other options that are available to you. Instead of being in this study, you could:

- choose to be treated with radiation or with drugs already approved by the FDA for your disease
- choose to take part in a different study, if one is available
- choose not to be treated for cancer but you may want to have comfort care to relieve symptoms.

You should discuss with your doctor your other choices and their risks and benefits.

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

The results of the standard tests performed as part of the research are available to you as part of your medical record.

In addition, when we are examining your DNA, it is possible that we could find changes in other parts of your DNA that are not related to this research. These are known as "incidental medical findings":

- Changes in genes that are related to diseases other than cancer
- Changes in genes that are not known to cause any disease. These are known as normal variations.
- Changes in genes that are new and of uncertain clinical importance. This means that we do not know if they could cause or contribute to a disease or if they are normal variations.

Since the analyses that we perform in our laboratory are not nearly as sensitive as the tests that are performed in a laboratory that is certified to perform genetic testing, the genetic changes that we find may or may not be valid. Therefore, we do not plan to inform you of all of the genetic results of testing on your tissue and blood that is performed in our research lab. However, in the unlikely event that we discover a finding that is believed to be clinically important based on medical standards at the time that we first analyze your results, we will contact you. This could be many years in the future. We will ask you to have an extra tube of blood drawn to verify the findings we have seen in our lab. If the results are verified, you will be re-contacted and offered genetic counseling here at NIH (no charge) or referral to an outside genetic healthcare provider (at your expense) to discuss the results.

EARLY WITHDRAWAL FROM THE STUDY

Your doctor may decide to stop the study for the following reasons:

- if you are found to be ineligible for the study
- if he/she believes that it is in your best interest
- if your disease worsens or comes back
- if you have side effects that your doctor thinks are too severe
- if you need treatment with a medication that is not permitted on the study
- if you become pregnant
- if new information shows that another treatment would be better for you
- if you do not follow the study rules
- if the study is stopped for any reason

In this case, you will be informed of the reason your participation in the study is being stopped.

After study drug is stopped we would like to see you for a safety visit 30 days after your last dose.

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 Karyopharm Therapeutics, Inc 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 MDS 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).

One way that we may share your data is by putting it into a large database called a repository, which is a way to make it widely available to the research community. If we do place your data in a repository, it will be labeled with a code, (not with your name or other information that could be used to easily identify you). Even though it will only be labeled with a code, some types of data, in particular data about your genes (called genetic or genomic data), can be used to figure out who you are, although this is difficult to do, and we think it is unlikely to happen.

The data in the repository will only be available to qualified researchers. These researchers must receive permission before they are allowed to access the data. Before receiving the data, the researchers must promise that they will not try to figure out the identity of the research participants.

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

Information about all the people (including you) in this study may be combined to create what is called summary information. The summary information may be placed in a database and shared in scientific publications. This information will help the researchers understand if some patterns are more common than others among everyone who was a part of this study. The summary information will be available to anyone without the need for any permission. The risk of anyone identifying you based on this information is very low.

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.

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 who 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.

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.

PAYMENT

Will you receive any type of payment for taking part in this study?

You will not receive any payment for taking part in this study.

REIMBURSEMENT

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

On this study, the NCI will reimburse the cost for some of your expenses such as those for hotel, travel, and meals. Some of these costs may be paid directly by the NIH and some may be reimbursed after you have paid. The amount and form of these payments are determined by the NCI Travel and Lodging Reimbursement Policy. You will be given a summary of the policy which provides more information.

COSTS

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.

- If some tests and procedures are performed outside the NIH Clinical Center, you may have to pay for these costs.

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 KPT-8602 developed by Karyopharm Therapeutics, Inc. 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
- The study Sponsor, Center for Cancer Research or their agent(s)
- Qualified representatives from Karyopharm Therapeutics, Inc., who produces KPT-8602

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.

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, about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Alain Mina, MD, alain.mina@nih.gov, 240-858-7625. 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

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: _____.